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ANDRÉ CROTTI ISSUE

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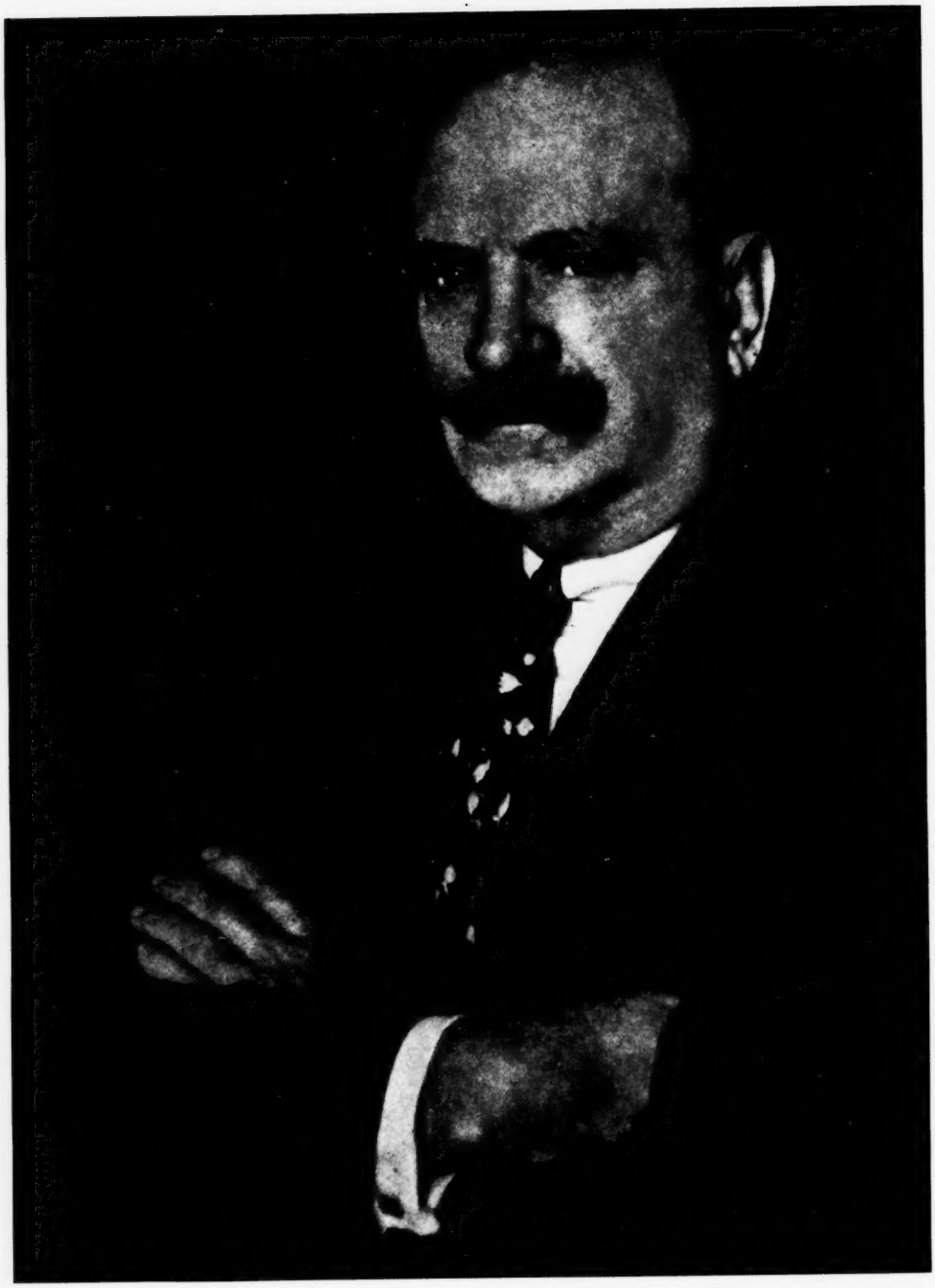

Dr. André Crotti

André Crotti, the Surgeon

IT HAS always been my philosophy to say appreciative words about a man while he is still living, and there is no man whom I would rather say them about than André Crotti. Our relationship began with the first meeting of the American Goiter Association, 1923, and in the years since then my admiration for him has continued to grow.

It is indeed a privilege to edit this issue of the *Journal of the International College of Surgeons*, which is dedicated to a great surgeon—André Crotti. Some of the outstanding authorities in surgery in this country and in Canada were invited to contribute to this issue of the *Journal*, but, unfortunately, lack of time prevented several from participating. However, they all expressed their sincere admiration for the man whose work in the surgical field is world renowned.

Dr. André Crotti was born in Buenos Aires, Argentina, Aug. 14, 1873. His parents were M. Charles and Mme. Marie Bisi Crotti. He received his education at the College of Saint Michel, Fribourg, Switzerland, and graduated from there with the degree of Bachelor of Lettres. In 1900, he received his medical degree from the University of Lausanne, Switzerland, and in 1902, after presenting a thesis, he was awarded his degree of Doctor in medicine. Following his graduation he became first assistant to Professor Stillings of the Pathological Institute, University of Lausanne, where he remained for about three years. He then became assistant to Professor Roux of the University of Lausanne, remaining there for four years, after which time he spent two years as assistant to Prof. Theodore Kocher of the University of Berne.

In 1902, Dr. Crotti was married to Marie Louise Gwynne of Columbus, Ohio, and two children were born to them—Mary Elizabeth, now Mrs. Maurice Gray Buckles, and André Jean, deceased.

Dr. and Mrs. Crotti came to the United States in 1908 and took up their residence in Columbus. Dr. Crotti matriculated at the Starling-Ohio College, graduated in 1908, and was licensed to practice medicine in the State of Ohio. He thus began the practice of surgery and has remained in this field since.

In December, 1913, he became a naturalized citizen of the United States of America.

For several years Dr. Crotti held the positions of Associate Professor of Anatomy and Professor of Clinical Surgery, Ohio State University, Columbus. He is a Past-Regent of the American College of Surgeons, Ex-President of the International College of Surgeons (1941-42), Past-President of the U. S. Chapter, International College of Surgeons, and recently was made President-Emeritus of the International College of Surgeons (1948).

He is a Fellow of the American College of Surgeons; the American Goiter Association; American Association of Obstetricians, Gynecologists and Abdominal Surgeons; the American Medical Association; Ohio State Medical Association; Columbus Academy of Medicine; Columbus Club. He is on the staff of Grant hospital, Mt. Carmel hospital, St. Francis hospital; and he was for many years Staff Surgeon at Children's hospital.

In 1921, he and Mrs. Samuel L. Black, Sr., founded the Columbus Cancer Clinic, and for 25 years Dr. Crotti was the medical director of the Columbus Cancer Clinic, which was the first clinic of that type founded in the United States. In 1948 he was made Medical Director Emeritus of that clinic.

As Dr. Theodore Kocher's assistant Dr. Crotti early became interested in the subject of goiter. With the tremendous amount of material available in his country, he had a splendid opportunity to study all phases of thyroid disease, and it was there that he gathered much of the material and knowledge that later enabled him to prepare his splendid treatise on this subject. He has written extensively on all subjects pertaining to his work, especially concerning goiter and cancer, the most notable being his publication, "Thyroid and Thymus," first published in 1918, revised in 1921 and re-published with extensive revision and additions in 1938 under the title "Thyroid, Parathyroid and Thymus." The scope of this great book was perhaps the most

comprehensive volume ever written on thyroid. It remains today one of the outstanding books on the subject. While in some aspects, it may not be in accord with the views of some American authorities, it is so comprehensive and so valuable that no student of this subject can afford to be without it.

Dr. Crotti was never one to favor the iodine deficiency theory as a cause of goiter, but instead has sought to prove that goiter is the result of a fungus. He did a great deal of research work in this field, and the papers which he has presented before the medical profession have always invoked much interest.

As a technician Dr. Crotti has few peers. It has been my privilege to see most of the leading thyroid surgeons on this continent at work, and Dr. Crotti's skill and judgment, his rapidity of dissection and his dexterity is rated with the best.

During World War I, he served as a Major in the United States Medical Corps, 1918–19. He has been decorated by the French, Italian and Polish governments. He resides at 1592 E. Broad St., Columbus, O., and maintains his offices at One S. Fourth St.

At the annual meetings of the American Goiter Association, of which Dr. Crotti is a past-president, we have all profited by the learned discussions which the old master has contributed. Yet one of the qualities I like best about André Crotti is his great capacity for friendship, his loyalty and his devotion to his friends.

ARNOLD S. JACKSON

André Crotti, the Man

I HAVE been requested to speak, in this issue of the Journal of the International College of Surgeons, of Dr. André Crotti, the man.

I have known him long and well. Having worked together as friends and fellow-surgeons, and as pioneer sodbreakers for the International College of Surgeons, I know him so well that I want every member of our great organization to see him and understand him as I do.

Dr. Crotti's physical appearance is striking —tall, erect, with a massive cranial architecture and penetrating eyes. Even his characteristic mustache has a personality of its own, as it expresses his moods with the eloquence of Toscanini's baton. He is as mild as a spring breeze until aroused by some challenge or injustice; then he becomes a volcano. He reacts like the keyboard of a sensitive Steinway to the fine touch of the soft pedal, but he responds equally as quickly to a devastating fortissimo when stirred by emotion. He never fears combat; he can dip his pen into vitriol as well as into mellifluous ink. But once one has his confidence, or has proved by his deeds the value of his friendship, André Crotti makes a paradise of that friendship. Those of us who have been fortunate enough to visit him, and those who have basked in the warmth of his family life, will attest to his kindness of heart. He is as charming a host as he is a rare connoisseur of the finer things of mundane existence.

He is a deeply religious man, but free from prejudice—those who truly love humanity cannot be prejudiced. "Give me the man," he often expostulates, "and I do not care where he worships, as long as he worships sincerely." We have often discussed racial and religious problems together, and I find him always magnificent in his anger against those small souls who summarily make religious belief, or intensity of skin pigmentation, a basis for prejudice, hate, or discrimination. On the other hand, he chooses his associates, social and otherwise, carefully, and is wisely selective as well as deliberative before concluding his course of action.

We were walking along the shore of Lake Michigan one evening while I visited him at his summer home. It was a starlit night. A full moon bathed the countryside in almost unreal beauty. Silence everywhere. "The mystery of it all," he mused. . . . "Divine architecture . . ."

I replied in the words of a Negro poet, a patient of mine, who wrote:

"Benny Goldblatt kneels in a synagogue to chant solemn praises to a frowning Jehovah flanked by Isaac and Abraham

"Ahmed Tagore lifts his hands at midday to a watchful Allah pointed out by Mohammed

"Samuel Middlebrooks prattles of a Christ Jesus who washed away his sins. . . . Samuel Middlebrooks sings loud hosannas to a Holy Trinity at the Wednesday night prayer meeting of the Second Baptist Church

"Wun Chong burns incense to a frozen faced Buddha who keeps his eye on the strength and weakness of all mankind

"Four omnipotent, omnipresent gods

"Which one made me? . . . Or was it any?"

Silence again. Crotti broke it. "The answer is all around us. . . ." "Yes," I retorted, "only a divine genius could have done it." "And a long time before those omnipotent gods were ever spoken of," he added.

* * *

I first met Dr. Crotti about fifteen years or so ago at the Grant Hospital in Columbus, Ohio, where he still lives and practices. We dreamed and worked together for the growth of my brainchild, the International College of Surgeons. Dr. Crotti labored with me and carried high the torch which I had lit, for he was elected the first president of the United States Chapter, and later, the second international president of the International College of Surgeons. While he was president of the United States Chapter, he wrote the *Constitution* which governs the activities of the College, both international and national. He founded the Journal, which in this issue honors his work and himself, and he designed the diploma which is given to every member, both

its art work and its French text. Dr. Crotti's services to the College have been invaluable and indefatigable and should never be forgotten.

Perhaps I can best tell you about that by quoting from my autobiography, published a few years ago, in which I wrote of Crotti:

"To this fine and sincere man the debt of the International College of Surgeons is great, indeed. It was he who chose its motto: *'Pro omni humanitate,'* and he who gave to it the perfect aphorism in which to express its highest ideals—the words of Louis Pasteur: *'La science n'a pas de patrie, parce que le savoir est le patrimoine de l'humanité, le flambeau qui éclaire le monde.'*

"Those sentiments are more than words to Crotti, whose life is guided by deep religious conviction and generous love for mankind.

". . . He had been assistant to the famous Roux of Lausanne and to the equally famous Kocher of Bern. His work on the thyroid has brought him international fame. And he is a cultured gentleman. The atmosphere which pervades the home where he lives with his talented and charming wife is one of high devotion to the best things of life, to truth and beauty and grace of living.

"Crotti succeeded Jirasek as president of the International College of Surgeons. He was naturally one of the first men I talked with on my return from Europe in the fall of 1937, and I was thrown even more closely in touch with him during the years that followed than I had been in the years that preceded. The association was always a joy and an inspiration."

* * *

Now, after fifteen years of association, I can only repeat those words with greater emphasis. André Crotti is a fine friend, a fine surgeon, and a fine American. He likes to see truth mirrored as it is—he is an objective man. Once a fine contemporary painter did his portrait in the "modern manner." Dr. Crotti considers the picture a caricature. "That is not I," he said. "Not by the farthest stretch of imagination can I see myself in this portrait. It is not true, and I like truth in any endeavor." Of diplomacy, so-called, he tersely remarks, "Diplomacy is duplicity, and I hate duplicity."

* * *

The hungry will never be turned away from his threshold unsatisfied, the heartsick without solace, or the weary without rest.

It was my pleasure to spend a day recently with him. . . . He is the same Crotti, with the same physical charm, the same sentiments, and the same eloquent mustache.

* * *

Here is a fragmentary pen portrait of André Crotti, the man, as I know him. He deserves the best from Him who guides our destinies, and may he receive it in plentitude, ad multos annos.

Max Thorek

COLLEGE INTERNATIONAL DES CHIRURGIENS
GENEVE

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Original Articles—Thyroid Surgery

Thyroiditis: Diagnosis and Treatment*

JOHN HERTZ, M.D., D.Sc., F.I.C.S.
COPENHAGEN, DENMARK

"A hundred hearings do not equal one seeing."—*Old Chinese proverb.*

"Like a drop of oil, it spreads and infiltrates all the organs."—*A. Crotti,* concerning Riedel goiter.

ACUTE thyroiditis was first recognized late in medical history. It was mentioned in the year 1800 by the Danish physician, Henrich Callisen under the name of "thyreoadenopyosis."

The history of chronic thyroiditis is more confusing. The classic account dates from 1896, when Riedel described the iron-hard goiter which was to bear his name (Fig. 1). It must not be overlooked that at least two previous descriptions exist, viz. Bowlby's (1884) of an "infiltrating fibroma" which undoubtedly corresponds to Riedel's type, and the "fibroid enlargement" described by Semple (1868), which probably represents the same entity. In 1912 Hashimoto introduced the histologic entity "struma lymphomatosa." In 1929 Williamson and Pearce described a condition designated as "lymphadenoid goitre," also covering mainly a histologic picture, both included in the French name "thyroidose lymphadinoide" (Weyeneth and Chanal). An excellent account of the more acute form of chronic thyroiditis, the giant cell or pseudotuberculous form, was given by deQuervain and Giordanengo in 1936.

CLASSIFICATION

This paper, like that of Simmonds', lists the chronic forms of thyroiditis, which are highly interesting to the surgeon, under the general heading of *cirrhosis.* The great difficulties of making a final classification are fully appreciated; for this reason the terminology refers only to the clinical and histologic aspects. Heavy academic duels have been fought for and against the unitarian conception first supported by Ewing's great authority in 1922; there can be no doubt that several facts are clearly in favor of this view, especially the pictures revealed in some of the extremely few published cases of recurrence after thyroidectomy for chronic thyroiditis (Heyd and Rosen). Several contributions to the solution

*From the Surgical Department, Karolinska, sjukhuset, Stockholm, Sweden.

of the problem have been given by Crile, Jr., Marshall, Meissner and Smith, Patterson and Starkey, and Schilling.

"Struma lymphomatosa" was considered a clinicopathologic entity of unknown cause while the fibroid form and the giant cell variations were taken to be late manifestations of an inflammatory process. In one case, in which changes corresponding to "struma lymphomatosa" and to the subacute nonspecific reaction appeared simultaneously, Schilling gave a rather peculiar explanation according to which the nonspecific lesion was superimposed on the already existing "struma lymphomatosa." This explanation is not very convincing. The question cannot be considered solved as yet.

The difficulty of making a proper classification may also, according to Wijnbladh, be ascribed to the fact that the thyroid gland has only a limited number of manifestations—a limited number of cords on its instrument, so to speak—alterations in the epithelium, lymphocytic infiltration and proliferation of connective tissue. The solution of the problem is still waiting and it depends on actual research rather than on academic discussion.

FREQUENCY OCCURRENCE

Thyroiditis is a rare disease. In the Karolinska sjukhuset, Stockholm, 1051 patients with lesions of the thyroid gland were treated between 1940 and 1947. There were five cases of acute and subacute thyroiditis, one of fistulous thyroiditis and two of chronic thyroiditis. These figures give an incidence of 0.5 percent for acute thyroiditis and 0.3 percent for chronic thyroiditis.

ETIOLOGY

It has been emphasized that the thyroid seems to possess a definite resistance to any local infection (Womack).

From an etiologic point of view, thyroiditis is a most variegated condition. Acute thyroiditis may occur as part of a common infectious or septic disease (I. Holmgren), or it may set in apparently as a lesion *per se*. Most frequently it is of hematogenic origin, and it would seem that infections in the upper respiratory tract, play an important role in this respect as stated by Berri, Bothe, Case, Derbyshire and Gray (Case 4).

Dental focal infection also has been held responsible as reported by Hagenbuch, Pedigo and Abramson, and Thorburn (Case 2). Records show cases in which the lesion appeared as direct extension from the surrounding tissues, e.g., a laryngeal necrosis after diphtheria (Janney) or pleuro-pneumonia in an adjacent lobe (Kirschbaum and Rosemblum).

Chronic thyroiditis may arise out of the acute condition as was stated so lucidly by Crotti. Nonsuppurative thyroiditis is only one stage in a process and there is no means of knowing beforehand what course the process will take. Calling the nonpurulent stage a disease *sui generis*, therefore, does not seem rational.

The cause is still obscure, and many possibilities have been suggested, from true neoplasm to chronic infection, specific or unspecific. DeCourcy considers chronic thyroiditis the result of previous perithyroiditis which has caused partial obstruction of the vessels leading to the thyroid, a process comparable to compensatory fibrosis of the kidney after constriction of the renal blood supply (Goldblatt). Vaux's conception assumes cirrhosis of the thyroid to be a process of involution similar to senile involution of the prostate and the mamma, a viewpoint hardly tenable in view of the occurrence of the former condition in patients age 19. "The gland burns itself out due to the demands of the body" (Pedigo and Abramson).

A morbid condition of the entire lymphoid system is suggested by one of Crile, Jr., cases, in which autopsy revealed generalized lymphoid hyperplasia.

Parmley and Hellwig ascribe lymphadenoid goiter to a disturbance of the normal cycle of thyroid activity (colloit secretion and release).

A very interesting case from an etiologic point of view has been reported by Ollgaard. The patient was a 49-year-old woman who died of typical Simmonds's disease with atrophy of the pituitary gland. Autopsy further revealed a moderate goiter of the Riedel type. It is impossible to decide whether thyroiditis was a consequence of the lesion in the hypophysis or a cryptogenetic disease of the thyroid gland.

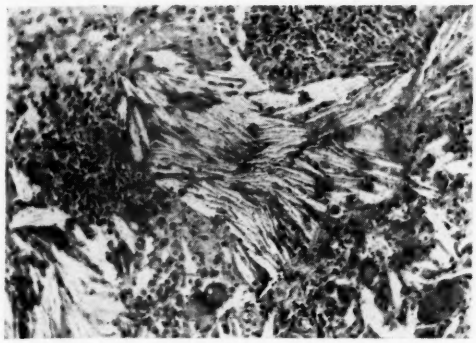

Fig. 1. Photomicrograph (X100) of fistulous thyroiditis with crystals of cholesterol (Case 6).

Thyroiditis develops comparatively frequently in association with pre-existing goiter. In this paper no attempt has been made to distinguish between this so-called "strumitis" and thyroiditis.

PATHOLOGIC PICTURE

Thyroiditis is generally confined to one lobe of the thyroid gland, most frequently the right (de Quervain). In some instances it originates in one lobe and progresses to the other; this is the migratory or creeping type (Case 2). The picture of the acute thyroiditis is essentially the same as that of all acute infections. In *case 6,* a chronic fistulous process resulted and the microscopic specimen revealed granulomas containing a considerable amount of cholesterol (Fig. 1). In this connection one of Schilling's patient's may be mentioned in whom a pseudoxanthoma elasticum associated with angioid streaks on the retina was observed in addition to the thyroid cirrhosis.

The microscopic picture of thyroid cirrhosis of the Riedel type (Fig. 2) is dominated by a dense fibrosis, often to an extreme degree; there is infiltration with lymphocytes and plasma cells; mononuclear cells as well as eosinophils have been observed (Grolitsch). Like a drop of oil (Grotti) or a slow fire (Patterson and Starkey) the cirrhosis spreads over the gland and all the organs of the neck forming a mass in which everything has been solidified. In a number of cases it is characterized by cellular aggregates resembling foreign body giant cells (de Quervain and Giordanengo's classic description of cases in which it bore a close resemblance to tuberculosis). The Hashimoto type is dominated by immense infiltration with plasma cells and lymphocytes, and the epithelium presents acidophilic degeneration.

CLINICAL SYMPTOMS AND DIAGNOSIS

Acute thyroiditis may appear at any age, although it is most frequent between the ages of 20 and 40 years. The incidence in men and in women is equal. The clinical chart exhibits a characteristic condition: a sudden onset with chills, lassitude, malaise, headache, fever and a feeling of pressure in the neck, which is aggravated by stretching. Very early in the disease dysphagia (Case 2 and 5) may set in as well as dyspnea, which may lead to stridor

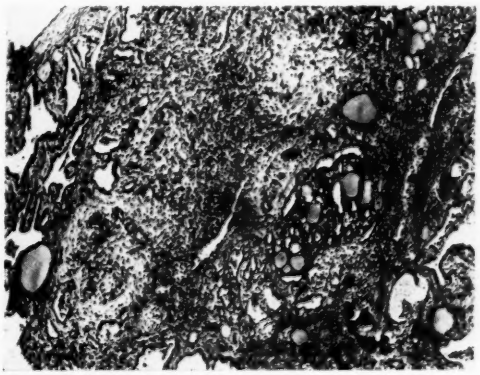

Fig. 2. Photomicrograph (X75) of Riedel type of thyroid cirrhosis (Case 8).

and in certain cases may even call for tracheotomy (Robertson).

These attacks of suffocation may be due to dislocation of the trachea or to edema of the glottis. Often there are sharp neuralgic pains in the branches of the cervical plexus, radiating to the homolateral ear and arm, to the neck and to the trunk. They are often caused by the dysphagia. In some cases hoarseness may set in because of an accompanying largngitis or paralysis of the recurrent nerve caused by a perforation (posteriorly) of the process. Generally there is also cough with blood stained sputum. Pressure symptoms from other organs occur but rarely. Compression of

the veins may lead to cyanosis, vertigo and epistaxis.

At examination the patient is often distressed, bending the head forward and toward the affected side, especially when swallowing. Gradually a swelling arises corresponding to the thyroid or to the lobe involved. It appears comparatively late owing to the deep location of the gland. It is of moderate size and most frequently hard, but sometimes somewhat elastic. It is tender and may be adherent to its surroundings; it moves up and down during deglutition; palpation may cause neuralgic pains.

The disease may give rise to hyperthyroidism as in *case 1*. It may even simulate exophthalmic goiter. These symptoms will subside when the thyroiditis has been cured. An interesting case has been reported by Bartels, in which thyroiditis developed in a patient with myxedema. The metabolic rate rose to the normal level but returned to the lower values when the thyroiditis regressed. Quite another picture is seen when the swelling of the thyroid gland makes its appearance in connection with some infection, especially influenza or rheumatic fever, when a complete thyrotoxic syndrome may develop within a few weeks (I. Holmgren).

In about 25 percent of cases the acute thyroiditis is reabsorbed, often very slowly; when it is left alone abscess formation most frequently results, and the clinical course is more serious. The symptoms often overlap; the pain increases; the fever continues intermittently; signs of increasing compression associated with stridor arise (Case 5); the skin may be adherent to the tumor and become red (Cases 3 and 5); fluctuation is rarely observed.

The abscess is often located posteriorly (Bothe) and may perforate into the trachea, the pharynx, the esophagus (Case 5), the large vessels, the pleural cavity, or posteriorly, extending into the deep spaces of the neck and into the mediastinum (Case 5). Perforation through the skin gives rise to fistulas (Case 6).

The prognosis is very favorable in those cases in which there is resolution of the process. It may regress and heal with a slight suppression of the glandular function, or hyperthyroidism may result as has been mentioned. Besides internal perforations, which often make the prognosis very gloomy, even lead to catastrophe (Case 5), other serious complications, such as edema of the glottis and laryngeal perichondritis, may develop and darken the prognosis.

Differential diagnosis is easy. Hemorrhages in the thyroid gland may give rise to sudden swellings, but the absence of fever makes a mistake impossible. Some malignant tumors grow rapidly enough to resemble an acute inflammation; this is most lucidly illustrated by Billroth's classic case and Hallstrom's more recent one, in which a malignant tumor grew so rapidly that incisions were made to relieve an acuate inflammation. Crotti has mentioned a similar case in which however, the proper diagnosis was made. Further confusion may arise in cases of phlegmons in the neck and in cases of tuberculosis and syphilis. These diseases are too infrequent to fall into the line which counts in this connection.

ACUTE THYROIDITIS: REPORT OF CASES

Case 1: Female, age 47. This woman, 20 years ago, had a goiter which disappeared after treatment with drugs, suffered 10 years later from nervous symptoms. Three weeks before admission to the hospital she noted a swelling on the neck corresponding to the previous goiter.

Examination revealed a firm and tender diffuse goiter which was not adherent. She presented no typical thyrotoxic symptoms, but she was nervous and there was gross tremor. The blood pressure was 160/110. The metabolic rate was plus 18, the sedimentation rate 90. The blood cholesterol was 138 mg. per 100 cc. Urinalysis, blood counts, and the level of nonprotein nitrogen were within normal limits. An x-ray of the neck and chest was normal. A later blood count showed hemoglobin to be 67 percent, red blood corpuscles—4.3 million, white blood corpuscles—4000, neutrophils—56 percent, basophils—2 percent, eosinophils—2 percent, lymphocytes—40 percent and large monocytes—2 percent.

During the first six weeks fever was continuous at about 101-102 F. Sulfathiazole was given (1 gm. five times daily during two weeks) without any definite effect. After five weeks stay in the hospital, the temperature declined to normal; also the sedimentation rate decreased and was 61 when she left the hospital. The goiter was still firm but not tender. The basal metabolic rate was plus 13.

Comments: In this case there was acute strumitis, the cause of which is unknown. The patient

had slight thyrotoxic symptoms and a slightly elevated metabolic rate. Sulfa drugs were without definite effect, but the disease gradually subsided and the patient was discharged in good condition.

Case 2: Female, aged 48. She had a severe dental infection from the third molar in the right mandible, with continuous pus formation, sequestration and lymphadenitis even after extraction of the responsible tooth. Two months later she suddenly had sharp pain in the right side of the neck, irradiating to the right mandible; dysphagia and probably fever. Furthermore, a swelling was observed on the right side of the neck. Later the symptoms moved to the left side.

Examination gave essentially negative results except for a sedimentation rate of 102 and a moderate diffuse swelling of the left thyroid lobe, which was firm and tender. It seemed to be adherent to the sternocleidomastoid muscle. The temperature was within normal limits. The blood pressure was 125/70, the blood calcium 11.2. Blood counts showed the hemoglobin to be 65 percent, red blood corpuscles—3.8 million, and white blood corpuscles—4,900. An x-ray of the chest and neck gave negative results. Penicillin was given, whereupon the symptoms subsided. At discharge the left thyroid lobe was still slightly tender.

Comments: In this case acute thyroiditis was present and it was obviously due to a dental focal infection. It was of the migratory or creeping type, starting in the right lobe and later moving to the left. Treatment with penicillin had a prompt and favorable effect.

Case 3: Female, age 29. She had had an abortion 10 days before and in the last four days had suffered from pain, some dysphagia and a swelling on the neck. On admission a diffuse, tender goiter was observed with some reddening of the skin. The temperature was 102 F. Blood counts showed a hemoglobin percentage of 71, red blood corpuscles—3.8 million and white blood corpuscles —5,600. The sedimentation rate was 107. An x-ray of the chest was negative. After some days of treatment with sulfadimin (1 gm. three times daily) the temperature was normal and the tenderness decreased. She was discharged in good condition with a sedimentation rate of 40.

Comments: In this case also the cause of the acute thyroiditis was not clear. It may have been due to the abortion, but this seems rather unlikely as the patient did not suffer from any pronounced puerperal fever. The thyroiditis subsided promptly in response to sulfa therapy.

Case 4: Female, age 33. For two weeks she had suffered from febrile rhinitis and a sore throat. A week later she had a cough, slight dysphagia, swelling and tenderness of the right side of the neck. The temperature was 100.9 F. She had been treated with sulfathiazole (5 gm. twice daily) and hot wet compresses. At entry she presented a firm, tender swelling, the size of a pigeon's egg, corresponding to the right lobe of the thyroid.

The metabolic rate was plus 8, the sedimentation rate—68. The blood pressure was 115/75. An x-ray of the neck and chest revealed no abnormality. The symptoms subsided and she was discharged in good condition with a very small, rather firm enlargement of the right thyroid lobe. The sedimentation rate was 60.

One month later she was still in good condition, with no demonstrable goiter and a sedimentation rate of seven.

Comments: In this case, acute thyroiditis followed an acute infection in the upper part of the respiratory tract. The disease subsided spontaneously, but the cure may have been due to the sulfa drugs administered previously to control the respiratory infection.

Case 5: Female, age 36. This woman for slightly more than a week had been suffering from increasing dysphagia and a rise in temperature, which was around 104 F. She also had some dysphagia and a tenderness of the neck.

On admission she had a tender, firm swelling corresponding to the thyroid gland with some reddening of the skin. She had several chills with a rise in temperature to 107.1 F. An incision was made to the thyroid gland but failed to reach pus or a more pronounced edema. An energetic treatment with sulfathiazole (1 gm. six times daily and Lugol's solution) was instituted. On the following day acute difficulties in respiration with cyanosis were overcome by means of oxygen given thru a nasal tube; a slight stridor persisted. Four days later there was a hemorrhage and some discharge of pus from the pharynx was noted. As the stridor and also the swelling and tenderness of the neck increased, intubation was attempted. Because of a sudden stridor a tracheotomy was also attempted; during these procedures which met with the greatest difficulties, she died.

Autopsy revealed abscesses in the right thyroid lobe; one especially large cavity presented itself, with perforation to the esophagus. Furthermore, there was a phlegmonous mediastinitis. A large amount of pus was found in the trachea and in the large branches of the bronchi.

Comments: In this case of acute suppurative thyroiditis the cause was also obscure. It was a severe condition and the sulfa treatment did not succeed because the incision failed to find the pus and provide a sufficient outlet. For this reason the abscess perforated posteriorly, obviously in part

thru the pharynx. At the same time the process progressed into the mediastinum.

CHRONIC THYROIDITIS

More variegated and complicated are the diagnostic problems relating to chronic thyroiditis. Analyses have been made of clinical charts and of the pathologic features in order to outline the setting of the different types, i.e., the Riedel type, the Hashimoto type, the de Quervain type and the chronic simple form. The results of these attempts are not convincing, and opinions differ.

Sudden onset has been reported (Braendstrup—Case 5—de Courcy) but is extremely rare. The disease may appear in any age group but is most frequent between the ages of 30 and 60. The onset may be insidious; the symptoms are few and vague. Some discomfort of the neck sets in. Then a slowly growing goiter appears spontaneously and gradually gives rise to pressure symptoms, with respiratory difficulties, cough and hoarseness. The last mentioned symtom may also be due to paralysis of the recurrent nerve; the dyspnea may occasionally require a trachectomy (Grolitsch). Sometimes neuralgic pains set in, irradiating to the homolateral ear and shoulder, or to the trunk. In a very few instances the condition has occurred without any noticeable goiter.

The goiter itself is hard and smooth, or it may have a diffuse, pebbly feel (Ficarra); in the later stages and in the pressure of extracapsular extension it is strongly adherent to the surroundings. The Hashimoto type is claimed to be without adhesions.

Hypothyroidism or hyperthyroidism may follow. Silght thyrotoxic symptoms were observed in 25 to 30 percent of the cases described here, and a picture resembling exophthalmic goiter has been met with in *Case 7* and *8*, (Braendstrup, Case, Gurkan, Hori, Rosen). There was a thyrotoxic picture with a considerable rise in the metabolic rate and a typical iodine response. Also a slight myxedema has been described (Ficarra, Haakon Rasmussen).

A case is on record (Reinhoff) in which the cirrhosis involved aberrant thyroid tissue situated in the supraclavicular fossa.

Recurrences of the cirrhosis are very rare, but cases have been reported (McClintock and Wright, Hertz, Heyd, Perman and Wahlgren, Rosen, Roulet, Schilling). The disease usually takes a benign course and the prognosis is favorable.

As will be evident from what has already been stated, the clinical diagnosis may be extremely difficult, as a gradually increasing, hard, smooth goiter, adherent to its surroundings may suggest many different lesions, e.g., cancer, tuberculosis, syphilis, lignous phlegmon, Hodgkin's disease or simple calcified adenomatous goiter.

A sedimentation rate which is normal or but slightly elevated, as well as a good general condition and the absence of metastases, may be of some aid. Negative results from the Wassermann test will rule out syphilis. A calcified adenoma is easily excluded by means of a roentgenogram. In cases of simple subacute thyroiditis only about five percent of a tracer dose of radioactive iodine is taken up (Crile, Jr.).

Consequently the old and eternal Chinese proverb, "a hundred hearings do not equal one seeing" holds good even here; in this intricate diagnostic puzzle, in which the paramount problem is to exclude cancer, it must be considered justifiable to resort to *seeing*, e.g., to an aspiration biopsy. The risk, chiefly emphasized in connection with biopsy is that it may aggravate the possible cancer, causing dissemination and formation of metastases. This risk has been highly overestimated (Engelbreth Holm); and even these objections do not exist as far as an aspiration biopsy is concerned.

The only real objection is the progression of a possible cancer through the tiny break made by the punch in the capsule of the tumor, and even this risk is exaggerated. If a cancer is to be present, treatment may be instituted accordingly and the risk eliminated; if the tumor is non-malignant the risk does not exist at all. Aspiration biopsy performed by means of Christiansen's rotating punch is a time-saving, safe and reliable procedure to obtain material for histologic examination when the immediate diagnosis is urgent. If Christiansen's rotating needle is not available, an ordinary 18 gauge needle and a record syringe will be entirely sufficient.

Practical experience also fails to show any alteration in the clinical behaviour of the tumor in cases in which malignancy has been ascertained (Hayes Martin, Memorial hospital, N. Y.). On the other hand, a real problem may arise from the difficulties in making the diagnosis even histologically (Graham). At operation also, the diagnosis may be very difficult. The consistency of the goiter, the white-spotted surface and the adhesions all indicate cancer. A histologic examination, by means of frozen section, at operation may be an aid. But the results obtained by a preliminary aspiration biopsy are far more reliable. Besides, harmful surgical intervention is thus avoided, which is also important.

CHRONIC THYROIDITIS: REPORT OF CASES

Case 6: Male, age 62. This man for 15 years had suffered from a goiter which had increased rapidly during the last three weeks of admission. An ulceration had appeared. There had been no complaints referring to compression. He had been treated with x-rays in another hospital.

Examination revealed a left sided nodular goiter, the size of two fists, with two ulcerations on the skin (Fig. 3). He presented no thyrotoxic symptoms, and the basal metabolic rate was plus 12. The larynx was felt to be highly dislocated to the right. The sedimentation rate was 18, the blood calcium 10.3, the blood phosphorus—3.8. An x-ray of the neck showed a dislocation to the right of the trachea, with a considerable compression, the lumen being only 5 mm. in diameter. Three biopsies failed to demonstrate malignancy or specific inflammation (Reuterwall) but revealed granulation tissue and firmer fragments consisting of epithelioid elements, fibroblasts and a considerable number of phagocytes.

A large number of foreign bodies, obviously crystals of cholesterol, were further observed and in connection with these foreign body giant cells (Fig. 1). Some necrotic parts were found, partly infiltrated with leukocytes. The treatment was confined to incisions and scraping of the foci, after which procedure the temperature rose to 101.8 F.

Chemical analysis showed the pus to contain 1.01 percent cholesterol. Sulfathiazole (1 gm. three times daily) was administered and the temperature subsided. More extensive surgical treatment was intended, but the patient failed to return. Eighteen months after discharge he was still in good condition.

Comments: In this case there was fistulous thyroiditis of undetermined origin. Obviously there was no question of a malignant tumor, as several biopsies failed to reveal malignancy and the course had been a benign one. Scraping of the foci brought about cure, at least temporarily. The microscopic picture was rather peculiar, revealing an inflammation with foci of granulomas containing a considerable amount of cholesterol. Chemical analysis also revealed a large amount of cholesterol in the pus.

Fig. 3. Thyroiditis with fistulas (Case 6).

Case 7: Female, age 59. She was admitted with a clinical picture closely resembling that of exophthalmic goiter, with a fine tremor, nervousness, perspiration, loss in weight (5 kg.) and loss of hair. For years she had noted a slight goiter and some dyspnea when walking.

Examination revealed a moderate goiter, a blood pressure of 135/80 and a basal metabolic rate of plus 82. The sedimentation rate was 11. Urinalysis, blood counts and x-ray of the chest revealed no abnormality. After preoperative iodinization, with a fall in the basal metabolic rate to plus 30, a subtotal thyroidectomy was performed. The removed gland did not present the picture of typical thyrotoxic goiter, but contained larger and smaller foci which were interpreted as foci of regression.

The microscopic specimen (Wilton) showed thyroid tissue with enlarged follicles covered by a low epithelium. Numerous foci were revealed consisting of epithelioid cells, with a few giant cells of the Langhans type and some infiltration with lymphocytes (Fig. 4). No necroses were demonstrated.

The examination failed to reveal tubercle bacilli. The vessels presented a pronounced calcification of the Monkeberg type in the media. No changes resembling exophthalmic goiter were demonstrated. Considering the postoperative course, the military foci may be interpreted as allergic tissue reactions. Six days postoperatively there was a swelling of the forearms and the hands, with pain and a temperature of 102.9 F., and an increase in the sedimentation rate to 62. The blood calcium was 11.3. Blood counts showed a hemoglobin percentage of 75, red blood corspuscles—4.4 million, white blood corpuscles—8,000, polynuclears—70 percent, eosinophils—1 percent, basophils—1 percent, lymphocytes—25 percent and monocytes 3 percent.

An x-ray of the hand was normal; x-ray of the lungs revealed some calcified primary complexes but no miliary dissemination. The symptoms subsided gradually in six weeks. At discharge she still had some swelling, especially corresponding to the metacarpophalangeal and the finger-joints, with some rigidity of the fingers. She was discharged in rather good condition with a basal metabolic rate of plus 1; the sedimentation rate was 30.

Comments: The condition in this case was interpreted as exophthalmic goiter and treated accordingly, was actually pseudo-tuberculous thyroiditis of the type described by de Quervain. A striking feature was the postoperative complication resembling primary chronic polyarthritis; the cause was unknown, but the possibility of allergic reactions cannot be excluded. Chronic polyarthritis developing some months after thyroidectomy has been described by Kirstein and Lovgren, who observed this complication in no less than 25 percent of 150 thyroidectomies.

In one case, Pedigo and Abramson have observed acute exacerbation of polyarthritis after thyroidectomy for a lmyphadenoid goiter.

Case 8:* Female, age 20. For six years she had a moderate goiter. The symptoms, which had increased during the last four months, consisted in slight dyspnea, nervousness, perspiration, tachycardia, some dysphagia and gross tremor. Pronounced dermographism was also present. At entry she presented a slight diffuse goiter. She had lost 12 kg. in weight. The metabolic rate was plus 40. The blood pressure was 125/65, the sedimentation rate—4 and the blood calcium—11.6. An x-ray of the chest and neck was normal and so was the electrocardiogram. The condition was interpreted as thyrotoxicosis; a subtotal thyroidectomy was performed after a preoperative iodinization with a fall in the basal metabolic rate to plus 19.

The postoperative course was uneventful, and she was discharged in good condition with a metabolic rate of plus 1. Two years later she was still in good health.

The microscopic specimen (Santesson) showed dense fibrous tissue with several blood patches of lymphocytes and plasma cells intermingled with thyroid epithelium. In several places, degenerative alterations were observed with destruction of the follicles. The follicles were of irregular shape and different sizes. Some larger follicles were observed in areas resembling adenomas. The epithelium was low cuboidal or low cylindric, but nowhere was it high cylindric. No lymphoid foci were demonstrated (Fig. 2).

Comments: In this case chronic thyroiditis (cirrhosis) was of several years' standing. It developed as typical thyrotoxicosis, with all the classic symptoms except exophthalmos, and was treated accordingly. There was a typical iodine response. Also the operation was performed according to that view. Microscopic study revealed the condition as cirrhosis resembling the Riedel type.

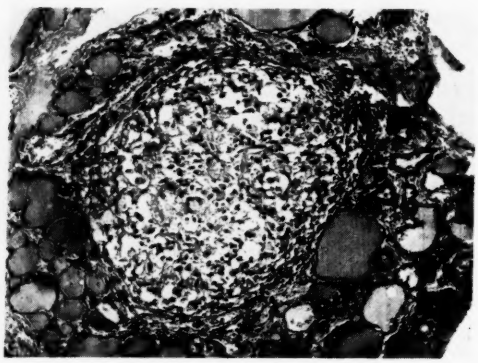

Fig. 4. Photomierograph (X165) of chronic pseudo-tuberculous thyroiditis (Case 7).

TREATMENT

The management of acute conditions of the thyroid gland profits by the new and most effective weapon given us in the sulfa drugs, penicillin, streptomycin and perhaps also aureomycin. Acute simple thyroiditis will often respond to a therapy consisting of confinement to bed, application of hot, wet compresses and chemotherapy with the aforementioned drugs. This treatment, if desired, may be supported by administration of oxygen (Womack).

*Besides this case, the author has previously published some illustrative cases on thyroid cirrhosis 16.

In a few instances, however, these drugs seem to be entirely without effect (Bartels, Derbyshire and Gray). In some of the cases (Case 2 and 3) chemotherapy had a promptly favorable effect, and the comparatively early spontaneous disappearance of the thyroiditis in another (Case 4) may be due to the previously instituted sulfa treatment.

In *case 1* the condition did not respond to sulfa therapy; in *case 5* the sulfa drugs were evidently without any effect at all because the incision failed to evacuate the abscess, and the process could never have been brought under control unless a sufficient outlet for the discharge had been obtained.

Inspired by the wave of enthusiasm following the inauguration of thiouracil in the treatment of thyrotoxicosis, King and Rosellini made an attempt to introduce this drug in the management of acute thyroiditis, in which the sulfa drugs have met with only slight success or with none at all. King and Rosellini even claim thiouracil to be a specific for acute thyroiditis. Lack of personal experience in this kind of treatment renders it impossible for the author to take any definite stand as to the efficacy of thiouracil in the treatment of these conditions.

The theoretic basis for its use seems rather obscure. The beneficial action of thiouracil is possibly due to its interference with the formation of colloit as the presence of which is considered responsible for the foreign body reaction.

The cases reported in King and Rosellini's publication also fail to convince one of the superiority of this therapy; the resolution in these cases of moderate thyroiditis began about a week after the institution of thiouracil. They have not attempted treatment with penicillin which seems to be more rational. Further experiences will have to be published before a definite evaluation of the thiouracil treatment is possible.

King and Rosellini also consider a diagnostic puncture desirable in order to ascertain the kind of bacteria responsible for the disease. This leads to another question: the therapeutic puncture with subsequent injection of penicillin combined with a general chemotherapy. In some few instances this treatment may be sufficient, as in the case reported by Torina and Caroccio. In Rischel's case of an abscess caused by Bang's abortus bacillus punctures without any supplementary chemoterapy brought about cure. Generally it would be a mistake to rely upon this procedure.

On the other hand, the eternal fundamental law of the surgery of ancient times, "ubi pus, ibi evacua," holds good also for suppurative thyroiditis. Surgical intervention must be resorted to, quickly and energetically. Two ways out present themselves; the abscess may be opened and drains introduced, a method proved sufficient in a number of cases (Berri, Bonney, Lambert Rogers, McQuillan and Breidenback). This procedure is not the treatment of choice. In most cases the outlet will be insufficient and the abscess will progress, possibly into the mediastinum, a grave consequence (Case 5). Total extirpation of the lobe involved will provide a sufficient outlet for the discharge, especially in cases of multiple abscess (Clute, Crotti, Hertz, Kocher). Consequently, this is my method of choice even if some technical difficulties are encountered, for these can be overcome.

The operation may be performed with local anesthesia, without depots on the superior thyroid artery; however, general narcosis by means of an intratracheal tube is preferable. If such a tube is not available, general narcosis should not be used on account of the risk of aggravating a possibly pre-existing stridor. Surgical treatment must, of course, be supported by adequate chemotherapy.

In cases of fistulous processes, scraping and drainage may give an excellent immediate result (Case 6). But even this procedure must be followed by a more extensive operation, that is, hemithyroidectomy.

In the management of cirrhosis, emphasis must be placed on relief of the mechanical effects of the goiter. For this reason, and perhaps also because, malignancy is suspected, treatment must be surgical even if it is empiric and unsatisfactory (Crile, Jr.).

If the diagnosis has been established by means of a punch biopsy the operation need not be a very radical one. Especially when the patient is in a hypothyroid stage, the less subnormal tissue removed the better. It is claimed to be advisable to give x-ray treat-

Data on Eight Cases of Thyroiditis

Case	Sex	Age	Diagnosis	Origin	Clinical Features	Sedimentation Rate	Hyperthyroidism	Treatment	Response to Chemotherapy	Result	Special Features
1	F	47	Acute simple thyroiditis.	Undetermined	Firm, tender goiter; continuous fever	90	Slight (metabolic rate plus 18)	Sulfathiazole	Uncertain	Cure	Pre-existing goiter.
2	F	48	Subacute simple thyroiditis.	Dental focal infection	Dysphagia; sharp pain; goiter moves from right to left side.	102	None	Penicillin	Good	Cure	Migratory or creeping form of cirrhosis.
3	F	29	Acute simple thyroiditis.	Undetermined	Pain; slight dysphagia; fever; tender goiter; reddening of the skin	107	None	Sulfadiamin	Excellent	Cure	
4	F	33	Acute simple thyroiditis.	Rhinitis	Fever; tender right-sided goiter	68	None (metabolic rate plus 8)	Sulfathiazole previously	Uncertain	Cure	
5*	F	36	Acute suppurative thyroiditis.	Undetermined	Dysphagia; fever; tender goiter; reddening of the skin; Stridor.	—	None	Incision, which failed to reach pus; sulfathiazole.	None	Death	Autopsy revealed mediastinitis and an abscess in the thyroid gland.
6	M	62	Fistulous thyroiditis.	Undetermined	Increasing goiter; later fistulas.	18	None	Incision and scraping		Cure, at least temporarily	Cholesterol containing pus; cholesterol granulomas.
7	F	59	Chronic thyroiditis (giant cell type).	Undetermined	Thyrotoxicosis giving typical iodine response	11	Marked (metabolic rate plus 82)	Thyroidectomy		Cure	Pseudotuberculous picture revealed microscopically Bacilli not demonstrated; postoperative complication resembling polyarthritis.
8	F	20	Chronic thyroiditis (fibrous type)	Undetermined	Thyrotoxicosis giving typical iodine response	4	Marked (metabolic rate plus 40)	Thyroidectomy		Cure (metabolic rate plus 1)	Cirrhosis (Riedel) revealed microscopically.

ment postoperatively; x-ray alone, as used by de Courcy and Lundbaek, with excellent results, cannot, however, be generally accepted when the relief of heavy pressure symptoms is urgent. The additional fibrosis produced by the reaction of irradiation may well increase the constriction of the trachea (Marshall, Meissner and Smith). Two cases are on record in which a lymphosarcome developed several months after a partial resection (Joll, Patterson and Starkey). Schilling in a comprehensive survey, stated that the Hashimoto type, revealed microscopically, will respond readily to x-ray treatment. The excellent x-ray response may even prove helpful in diagnosis. However, I am of the opinion that this procedure is more that outweighed by the aspiration biopsy.

Schilling is unable to judge the x-ray responses of granulomatous goiter, as this lesion often subsides spontaneously, but Patterson and Starkey claim that this kind of tumor also responds readily to x-ray. Consequently, in cases of Hashimoto type and granulomatous goiters, x-ray treatment should be given a trial.

Radium treatment also is said to have given good results in some instances (Maloney and St. George). In the treatment of the Riedel type, x-ray treatment has little to offer (Schilling, Crile, Jr., Patterson and Starkey).

As cirrhosis is considered to depend upon a low grade inflammation, the question of chemotherapy suggests itself. I have been unable to trace statements concerning chemotherapy in the available literature, but I am of the opinion that chemotherapy cannot replace surgical intervention as the condition represents cicatrices after inflammation, or late burnt-out stages. Nor can quick relief of compression be obtained by means of chemotherapy alone.

SUMMARY

After a brief survey of some historical data concerning thyroiditis, an account is given of the frequency of this lesion. The etiology and pathology of the disease are mentioned and it is emphasized that in one of the reported cases there was an inflammatory process, characterized microscopically by a large amount of cholesterol. A more comprehensive report of the clinical features and the diagnostic problems is given. The significance of an aspiration biopsy is strongly emphasized and this procedure highly recommended.

The treatment is also discussed. Acute simple thyroiditis should be treated essentially with chemotherapy, and in some few cases of the suppurative form, the treatment may be confined to puncture with injection of penicillin. The treatment in most cases of acute suppurative thyroiditis is surgical confined in some few instances to incision and drainage, but generally entailing extirpation of the lobe involved to prevent dangerous complications, especially extension into the mediastinum from arising. Also in cases of thyroid cirrhosis, the treatment consists of thyroidectomy, simply to relieve the often severe pressure symptoms. In cases of the Hashimoto type, and of granulomatous goiter, in which the diagnosis has been established by means of a punch biopsy, x-ray treatment should be given a trial. Also radium has been used and may be helpful.

RIASSUNTO

Breve riassunto storico delle tiroiditi, con particolare riguardo alla frequenza di questa malattia. Traendo argomento da alcuni casi occorsi alla sua osservazione, in uno dei quali l'esame microscopico a vera dimostra to la presenza di un processo infiammatorio con un largo accumulo di colesterina, l'A. ne discute l'etiologia e la patologia. Illustra il quadro clinico e prospetta i problemi diagnostici: si dichiara un coninto fautore della biopsia per aspirazione. In quanto alla cura, l'A. ritiene che nelle tiroiditi semplici la chemioterapia sia sufficiente. Nelle forme suppurative, solo pochi casi possono essere curati con la penicillina: nella maggioranza la cura e' chirurgica con incisioni e drenaggio nei casi piu' lievi, con asportazione del lobo suppurato nei casi piu' gravi onde evitare pericolose complicazioni e piu' specialmente una diffusione al mediastino. Nei casi di cirrosi tiroidea consiglia la tiroidectomia, se non altro per attenuare i sintomi di compressione. Nelle tiroiditi a tipo Hashimoto e nel gozzo granulomatoso consiglia un tentativo di cura con raggi X o con radium.

SOMMAIRE

Apres une étude brève de faíts historiques par rapport à la thyroïdite, l'auteur décrit la fréquence de cette lésion. L'étiologie et la pathologie de ces maladies sont mentionnées Dans un cas, il y avait une inflammation caractérisée microscopiquement, par une grande quantité de cholestérol. Un rapport compréhensif des symptômes et des problèmes diagnostic est donné.

La signification de l'importance de la biopsie aspiratoire est notée avec emphase et cette methode est hautement recommandeé. Le traitement est aussi discuté, Une simple thyroïdite aigüe sera traiteé essentiellement par chémothérapie et dans quelques cas de suppuration le traitement consistera dans la ponction avec injection de penicilline. Le traitement dans la plupart des cas de thyroïdite suppurative aigüe consiste en incision et drainage, quoique souvent il faille enlever la glande pour prévenir de dangereuses complications, surtout l'extension dans le mediastin. Aussi dans le cas de cirrhose thyroïdienne, le traitement consiste en thyroïdectomie, simplement pour soulager les symptômes sérieux de compression.

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Evaluation of the Present Treatment of Hyperthyroidism*

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DURING the past decade, two developments in the field of thyroid research have proved to be of far-reaching significance, namely, the discovery that the function of the thyroid gland can be suppressed by goitrogenic drugs, notably thiouracil and related compounds, and the demonstration of the value of radioiodine as a tool for study of thyroid function as well as a therapeutic agent in the treatment of some types of thyroid disease. By opening new approaches to thyroid investigation, these agents have been responsible for rapid and sound advances in our knowledge of the physiology of the thyroid gland, and both have contributed greatly to the effectiveness of the treatment of hyperthyroidism.

These developments have been spectacular and have been enthusiastically received by the profession. However, it is evident that these advances have not provided the final solution to the problem of goiter, nor has effectiveness of treatment yet reached the stage whereby established methods of treatment can now be discarded.

It is the purpose of this discussion to review our clinical experience with these agents at the Mayo Clinic, as well as the experience reported by others, and to attempt to evaluate their use in the treatment of hyperthyroidism.

GOITROGENIC COMPOUNDS

For many years it has been known that certain substances would produce enlargement of the thyroid gland in animals, but it was not until 1941, after the studies of several investigators, notably Mackenzie, Mackenzie and McCollum,[1] Riteher and Clisby,[2] Kennedy,[3] Griesbach and Purves,[4] and Astwood, Sullivan, Bissell and Tyslowitz,[5] that any progress was made in determining the mechanism by which sulfonamides and thiourea induce enlargement of the thyroid and reduction of its function. After the publication of Astwood's[6] report in 1943 on the control of hyperthyroidism in three cases of Graves' disease by treatment with thiourea in one case and with a related substance, thiouracil, in the other two, thiouracil became available to many investigators for use in treatment. Soon reports confirming the effectiveness of the drug were published.

Studies with radioiodine on animals treated with thiouracil followed. Thus, Larson and his co-workers[7,8] showed that the drug prevented all but small amounts of iodine from entering the gland. Rawson and his associates[9] found that the drug prevented proper utilization of iodine by the thyroid gland but that in spite of this action iodine, in large amounts, produced involution of the gland. Other studies, many of them involving the use of radioiodine, indicate that although iodine may be trapped by the thyroid under the effect of thiouracil, thyroid hormone is not formed.

The dramatic response of patients with hyperthyroidism to treatment with thiouracil led to use of the drug as a measure for preparing these patients for surgical treatment in some clinics, and as total treatment in others. When such treatment was used as the sole preparatory measure, incredibly annoying bleeding was encountered at operation which increased appreciably the technical difficulties of the operation. This problem was partially solved when it was learned that the administration of iodine, either during the preoperative period of preparation with thiouracil or for a period of two weeks prior to operation, would induce involution of the gland without interfering with the antithyroid action of thiouracil. Indeed, the use of iodine in many such cases results in a further drop in basal metabolic rate.

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It was soon discovered that the use of thiouracil was not without danger, for not infrequently toxic effects became manifest. Of these the most serious was agranulocytosis which occurred in about 2.5 percent of many reported series. It became apparent that the drug should be used cautiously and only when the patient under treatment could be kept under constant medical supervision. The introduction by Astwood and Vander Laan[10] of propylthiouracil (a compound less toxic than thiouracil) stimulated increased interest in this form of therapy.

While propylthiouracil is far superior to thiouracil for the treatment of hyperthyroidism, it is not free of toxic side effects, for the occasional occurrence of minor reactions requiring the discontinuance of the use of the drug[11] has been reported and at least two instances of agranulocytosis have been charged to it.

Several investigators have employed thiouracil or propylthiouracil as total treatment in the hyperthyroidism of Graves' disease. Although complete remission of hyperthyroidism in most cases can usually be induced in two to three months and apparently maintained as long as administration of the drug is continued, the incidence of recurrence of the disease after withdrawal of the drug is high. Thus, Williams[12] reported that two weeks to five months after administration of the drug was discontinued, 51 percent of his patients had had relapses. In a series of 17 cases reported by McCullagh and his associates,[13] the disease recurred in six, or 35 percent, in one week to 14 months after the withdrawal of the drug.

The high incidence of recurrence after treatment with goitrogens, the difficulty in keeping patients under prolonged observation and the occurrence of occasional untoward reactions, even from use of propylthiouracil, are the factors that have influenced us to confine the use of the drug as total treatment for hyperthyroidism to the occasional, unusual case in which no other form of treatment seems adequate or feasible. Furthermore, the relatively small but significant incidence (four to six percent), of malignant lesions in nodular goiters definitely contraindicates the employment of any nonsurgical method as total treatment for hyperthyroidism associated with adenomatous goiter.

As a measure of preparation for operation, propylthiouracil used concurrently with iodine has been valuable in reducing the operative mortality in those cases in which the patient is a poor surgical risk because of the severity of the hyperthyroidism or because of the presence of complications. The question arises whether there are reliable criteria by which the safety of the operation on patients with toxic goiter prepared by medication with iodine can be accurately judged. An analysis of the potential hazards associated with the surgical treatment of these patients reveals that they fall in two main groups:

1. The normal hazards inherent in any surgical procedure, such as those connected with operation on patients with nontoxic goiter. These are limited, for the most part, to technical errors.

2. The additional hazards incident to hyperthyroidism. These additional hazards in turn may be divided into two subgroups: (a) those associated with the development of an overwhelming postoperative hyperthyroid crisis, usually confined to cases of severe hyperthyroidism and (b) those related to the debility of the patient that results from the intensity of the disease, long-continued hyperthyroidism, advanced age or intercurrent disease.

On the basis of these potential hazards is it possible to gauge, with a reasonable degree of accuracy, the surgical risk for the patient with toxic goiter? As previously reported,[14] an attempt to determine this point was made by correlating the mortality with the previously recorded ratings of the hazards in a large number of patients with toxic goiter prepared with Lugol's solution. The grading of the operative risk was made on the basis of 1, 2, 3 and 4. The normal risk of the patient with nontoxic goiter was graded 1, and the normal risk of the patient with toxic goiter was graded 1+. The estimation of any additional hazard was added to the normal rating.

This survey illustrated that while it is not possible to foretell which patient will not survive the operation, it is possible from the clinical estimate of the hazard to select a

small group of patients whose ratings are adjudged moderately or greatly increased and from which 81 percent of the mortality will be derived.

The time required for effective preparation with goitrogenic drugs, of the patient who has Graves' disease, is two or three times greater than that needed for adequate preparation with Lugol's solution. The goitrogenic drugs are potentially toxic and since the operative risk in cases of mild or moderate severity, in which the patient is prepared with Lugol's solution is no greater than it is in cases of goiter unassociated with hyperthyroidism, it is our practice to confine the use of propylthiouracil to the cases of severe or complicated disease. The results of surgical treatment of patients with toxic goiter prepared as outlined have been excellent.

Thus, at the clinic in a recent series of 455 consecutive cases of exophthalmic goiter, in which thyroidectomy was performed, there were no deaths. In a similar series of 334 patients who had adenomatous goiter associated with hyperthyroidism, and who were operated on during the same period, two patients died. The mortality rate for the combined groups, comprising all the cases of hyperthyroidism, was only 0.25 percent (table 1). Subtotal thyroidectomy was performed as a single stage procedure in all the cases of exophthalmic goiter and in all but three of the cases of adenomatous goiter. In all these three cases technical difficulties, rather than inadequate preparation of the patient, constituted the factor which influenced the decision to perform the thyroidectomy in stages.

Data regarding the number of patients to whom the goitrogenic drug was administered are not readily available, but it is estimated that the number did not exceed five percent of the patients operated on. Those patients who were prepared with propylthiouracil for operation were, as a group, patients who were severely hyperthyroid, or who had complications which were being adversely affected by hyperthyroidism. In such cases prolonged periods of preoperative preparation seemed justifiable and the complete control of hyperthyroidism before operation was undoubtedly an important factor in the absence of mortality in the group. In rare cases, toxic manifestations of the drug necessitated return to older methods of preparation.

Although the number of cases in which we have used propylthiouracil in the preparation of the patient with hyperthyroidism for operation is small, we are confident that it has made a valuable contribution to preoperative treatment. Other measures of proved value introduced in recent years also have greatly contributed to reducing the mortality rate in all fields of surgery. Agents for controlling infections, such as the sulfonamide compounds and the antibiotics, are outstanding examples. In a group of 801 patients with nontoxic goiter who underwent thyroidectomy without any special preoperative preparation, there were no deaths.

RADIOIODINE

In recent years radioiodine has become an important tool in the study and treatment of thyroid disease. It has proved particularly profitable in the experimental laboratory as a means of investigating many important aspects of thyroid physiology. It has been used in in vitro experiments dealing with the synthesis of thyroid hormone, in numerous animal experiments dealing with the action of pituitary thyrotrophic hormone and with the site of action of various goitrogenic substances and in the study of numerous other problems involving the function of the thyroid.

Radioiodine may, however, prove to have its greatest promise as a means for studying thyroid function in man. Its use already has provided a considerable quantity of new information concerning the fundamental metabolism of iodine, the behavior of thyroid tumors and the action of antithyroid drugs. It is safe to predict that the careful administration of radioiodine tracers to patients for purposes of clinical investigation will continue to augment our present knowledge of thyroid disease. The value of radioiodine as a diagnostic agent is also becoming more and more apparent.

The use of radioiodine as a therapeutic agent in carcinoma of the thyroid has been, with few exceptions, disappointing. Grounds remain for hoping that means will be found which will make radioiodine more effective in this condition, but at the present time only

a small proportion of patients with malignant disease of the thyroid gland appear amenable to treatment with this agent.

Radioiodine has, on the other hand, proved to be an effective means of control in many cases of hyperthyroidism. Its use in this respect continues to be cautiously explored. At present, no serious ill-effects following the use of radioiodine have yet been reported, but concern over the possibility that untoward consequences of radiation might appear long after administration of radioiodine is an important factor that limits its more extensive use in hyperthyroidism.

Because of the unknown character of the radiation hazard in the treatment of hyperthyroidism with radioiodine, at the clinic we have deliberately limited the use of radioiodine to older patients for whom thyroidectomy is regarded as unduly hazardous because of some serious complication such as heart disease, and to cases in which repeated recurrences have followed previous thyroidectomies. The patients selected have, therefore, included a group in which the hyperthyroidism had proved itself resistant to other forms of treatment. Insufficient time has elapsed for accurate evaluation of the results of treatment of hyperthyroidism with radioiodine.

To date, however, the disease has been satisfactorily controlled by this means in more than 80 percent of the patients selected. The incidence of recurrences and of myxedema following use of radioiodine has, as might be expected, been found to be higher than is the incidence following thyroidectomy. In those patients in whom the disease has recurred, further doses of the isotope have controlled the disease. Much remains to be learned regarding the effective dose. Whether or not this can be gauged so accurately that recurrences or myxedema become less frequent, this substance will hold for some time an important place in the treatment of many patients in whom the risk of thyroidectomy would be excessively high even after preoperative preparation with propylthiouracil.

Patients with recurrent exophthalmic goiter in whom the thyroid remnant has not appreciably enlarged seem to us to be peculiarly suitable cases for treatment with radioiodine, as further surgical intervention will result in the removal of only minute amounts of thyroid tissue, and as these patients are particularly prone to recurrence of hyperthyroidism after treatment with antithyroid drugs. So, too, is the elderly patient with hyperthyroidism and serious heart disease a good candidate for radioiodine therapy, as no immediate risk has resulted in such cases, and late effects of radiation are not feared in such cases as they are in the young patient.

Radioiodine, either as a research tool or a

TABLE 1

Diagnosis	Cases	Hospital Deaths		
		Number	Percent	
Exophthalmic goiter	455	0	—	0.25
Adenomatous goiter with hyperthyroidism	334	2	0.6	
Adenomatous goiter without hyperthyroidism (including thyroiditis)	801	0	—	
Malignant disease	75	1	1.3	
Total	1,665	3	0.18	

Data on 1,665 consecutive cases of goiter (to January 1, 1948) in which thyroidectomy was performed.

therapeutic agent, is potentially dangerous and its use requires the same kind of precautions against the insidious and disastrous consequences of radiation for the patient, the physician and the technician as does the use of radium or roentgen rays. The application of radioiodine to clinical problems involves a large number of intricate and often highly technical problems, so that for a considerable time to come the safe use of this agent will be possible only when supervised by well-integrated research teams which include physicists, radiologists, biochemists, internists and surgeons.

SUMMARY

Propylthiouracil is a valuable drug for controlling hyperthyroidism, but because of its potential toxic side effects and because of the high incidence of relapses after its withdrawal, employment of this agent as the method of choice in the total treatment of Graves' disease has, in our opinion, not been established.

As a means of preparing the patient for operation, medication with iodine has proved adequate except for a small group of patients whose operative risk is high because of severity of hyperthyroidism or because of complications. For this group, treatment with propylthiouracil has been found to be very valuable as an additional measure of preparation. The surgical mortality rate for patients with toxic goiter prepared according to the above described method has been exceedingly low, namely, 0.25 percent.

Treatment with radioiodine has proved to be an effective means of controlling the disease in many cases of hyperthyroidism. The permanency of the results cannot now be determined. Until greater accuracy in gauging the dose is established and until the potential radiation hazard in the treatment of hyperthyroidism with radioiodine is known, we believe that caution demands that employment of this drug be limited to those patients for whom thyroidectomy is regarded as unduly hazardous.

We feel that thyroidectomy after either Lugol's solution alone or Lugol's solution and propylthiouracil preparation, is at the present time the most conservative method of treatment for the majority of patients with exophthalmic goiter. The short time needed for this method of treatment, the speed of control of hyperthyroidism, the high incidence of permanence of control, and the low incidence of morbidity and mortality make surgical treatment a method which must still be considered in most cases of hyperthyroidism and which will be the treatment of choice in many instances.

RIASSUNTO

Propiltiouracile e' una sostanza utile per il controllo dell'ipertiroidismo, ma le possibili manifestazioni tossiche e l'alta percentuale di recidive dopo la sospensione della cura impediscono di adottarla quale metodo di elezione per la cura del morbo di Graves.

Nella preparazione degli ammalati per l'operazione l'iodio conserva nella maggioranza dei casi i suoi diritti. Solo in un piccolo gruppo di casi, nei quali il rischio operatorio e' reso troppo grave dall'intensita' delle manifestazioni tossiche o da complicazioni, il tiouracile offre degli effettivi vantaggi.

La mortalita' operatoria nei casi di strumi tossici, preparati con questo metodo, e' scesa al 0,25%.

In molti casi di ipertiroidismo l'iodio radioattivo ha dimostrato un ottimo risultato sopra la malattia; ma sia perche' la durata dei risultati non e' stata ancora bene definita, sia perche' la determinazione della dose lascia ancora a desiderare, sia perche' i rischi della radio-attivita' non sono ancora sufficientemente noti, l'A. ritiene che questo rimedio vada riservato ai casi nei quali la tiroidectomia appaia troppo pericolosa. La cura chirurgica, intrapresa dopo la somministrazione sia di iodio, sia di tiouracile, rimane nella maggioranza dei casi il metodo di elezione perche' richiede poco tempo, controlla rapidamente ma prolungatamente i sintomi di ipertiroidismo, presenta una bassa percentuale di morbilita' e di mortalita'.

SUMARIO

En nuestra opinion la tiroidectomia con preparacion previa por la solucion de Lugol solamente o en conjuncion con la propiltiouracila es el metodo mas conservativo en el tratamiento de la tirotoxicosis en la mayoria

de los pacientes. Este tratamiento requiere poco tiempo, controla rapidamente las manifestaciones toxicas y da una alta incidencia de curaciones permanentes. Aun mas, presenta una mortalidad y morbilidad muy baja. Es por lo tanto el tratamiento de seleccion en la gran mayoria de los casos.

SOMMAIRE

Le propylthiouracile est un médicament de valeur pour le contrôle de l'hyperthyroïdisme, mais vu ses effets toxiques potentiels et aussi vu la haute fréquence des rechutes après la cessation de son administration, son emploi comme agent de choix dans le traitement exclusif du goître exophthalmique n'est pas definitivement établi. Comme moyen de préparer le malade pour l'opération, l'emlpoi de l'iode est adéquat, excepté pour le petit groupe de malades présentant des symptômes de risques opératoires élevés vu la sévérité de l'hyperthyroïdisme ou de ses complications. Pour ce groupe, le traitement avec le propylthiouracile a de la valeur comme mesure additionnelle de préparation. Les malades souffrant de goître toxique, préparés préopérativement par la méthode décrite ci-dessus, donnent un taux de mortalité très bas, à peu près de 0,25%.

Le traitement avec la radioiode s'est montré efficace pour contrôler beaucoup de cas D'hyperthyroïdisme. La permanence des résultats obtenue ne peut pas encore être déterminée. Tant qu'on ne sera pas définitivement renseigné sur la dose à employer et tant que les hasards potentiels de l'emploi de la radiation dans le traitement de l'hyperthyroïdismene sont pas connus. Nous croyons qu'il est mieux d'employer ce mode de traitement seulement pour les malades chez qui une thyroïdectomie nous paraît très dangereuse.

Nous sommes d'avis que la thyroïdectomie après l'emploi seul de la solution de Lugol ou avec la propylthiouracile est pour le moment la méthode la plus conservative pour la majorité des malades souffrant du goître exophthalmique. Le peu de temps requis pour ce mode de traitement, la rapidité avec laquelle l'hyperthyroïdisme est contrôlé, la haute fréquence de contrôle permanent et la basse incidence de morbidité et de mortalité, font que le traitement chirurgical est la methode doit être considérée dans la plupart des cas comme le traitement de choix.

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The Present Status of the Treatment of Hyperthyroidism

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UNTIL the discovery of the antithyroid effects of the derivatives of thiourea, subtotal thyroidectomy was the only means of controlling hyperthyroidism. Now propylthiouracil, developed by Astwood, has proved to be a relatively non-toxic drug and in adequate doses has been effective in controlling the hyperthyroidism of over 90 percent of the patients treated.[1] Although the hyperthyroidism often recurs promptly when treatment is withdrawn, some patients remain in remission indefinitely and appear to be cured.

The controversy between the proponents of propylthiouracil and those of thyroidectomy was at its height when radioactive iodine, first used in 1941 by Hertz[2] and independently by Hamilton and Soley,[3] became available in the form of I^{131}, and was distributed for experimental use by the atomic energy commission.

Propylthiouracil, thyroidectomy, and I^{131} each has its advantages and each seems well adapted to the treatment of certain patients with hyperthyroidism and less well adapted to the treatment of others. The purpose of this discussion is not to pass final judgment on the merits of the various forms of treatment now available but is rather to evaluate our present knowledge of their advantages and disadvantages.

THYROIDECTOMY

Thyroidectomy, after preparation with iodine, can be accomplished with a mortality rate of slightly less than 1 percent.[4,5] But if operation is deferred until the hyperthyroidism is completely controlled by the administration of propylthiouracil, and if the patient is further prepared by the administration of large doses of iodine for the last two weeks, the mortality rate of thyroidectomy falls to less than 0.2 percent.[5,6]

One of the factors in this reduction in mortality is the complete control of the hyperthyroidism prior to operation—a circumstance which reduces the risk to the level of that of thyroidectomy for simple goiter. A second factor is the ability of the surgeon to select the cases for operation and to treat by nonsurgical means those patients who are not good risks.

Although thyroidectomy is an effective means of controlling hyperthyroidism associated with Graves' disease as well as that secondary to nodular goiters, the incidence both of recurrent hyperthyroidism and of postoperative hypothyroidism is much higher following operations for Graves' disease than following those for nodular goiter. If a very radical subtotal thyroidectomy is done for this disease, the incidence of postoperative hypothyroidism will be in the neighborhood of 20 percent and the incidence of recurrent hyperthyroidism over a five to 10 year period in the neighborhood of three percent. If a conventional type of thyroidectomy is done, the incidence of hypothyroidism will be only about four percent. However, 15 percent of the followed cases will develop recurrent hyperthyroidism within five to 10 years.[5] Following operations for nodular goiter with hyperthyroidism the incidence of recurrent hyperthyroidism is almost negligible. Regardless of technic, myxedema does not occur unless a true total thyroidectomy has been done, and even mild hypothyroidism is rare.[5]

In view of this experience it is clear that thyroidectomy is a preeminently satisfactory treatment for nodular goiter with hyperthyroidism and is a somewhat less satisfactory answer to the treatment of Graves' disease.

The morbidity following operation for Graves' disease and following operations for nodular goiter is approximately the same. If the conventional technic of resection of the thyroid over closed hemostats is used, my own experience indicates that it is not possible to perform an adequate thyroidectomy without causing permanent damage to one recurrent laryngeal nerve in about three per-

cent of the cases and causing permanent tetany in at least 0.6 percent.[5] If the anatomic technic is used and the thyroid is rotated from its bed, the inferior thyroid artery ligated well lateral to the thyroid, and the recurrent nerve and parathyroids identified, the incidence of these complications is reduced to less than 0.4 and 0.2 percent respectively.[5,7]

From this summary it is apparent that in the hands of surgeons interested in thyroid disease, the mortality, morbidity, and end results of thyroidectomy for nodular goiter with hyperthyroidism are excellent and for Graves' disease are good, but somewhat less perfect.

Other factors associated with thyroidectomy that require consideration are:

1. The necessity for loss of work, hospitalization, and a relatively long period of detailed professional supervision.

2. The natural distaste of the patient for the discomfort and anxiety associated with an operation.

3. The minimum, but ever-present risk of incurring mortality or morbidity by operation.

4. The fundamental principle that if a more conservative treatment can give as good a result it is preferable to an operation from the standpoint of both patient and physician.

In favor of thyroidectomy are the following considerations:

1. The goiter is removed, a factor which may be of cosmetic importance and which may eliminate the remote possibility of a coexistent malignancy in a nodular goiter.

2. The results of treatment are prompt and definitive as compared with prolonged treatment with propylthiouracil.

PROLONGED TREATMENT WITH PROPYLTHIOURACIL

Propylthiouracil blocks the formation of thyroid hormone and in this way produces a physiologic instead of an anatomic thyroidectomy. It is not apparent why the hyperthyroidism does not always recur following a course of treatment with propylthiouracil because so far as is known, the underlying cause of the hyperthyroidism (i.e. the factor which drove the thyroid to hyperfunction) is not affected by the drug. Despite this fact long-standing and possibly permanent remissions of hyperthyroidism may be seen after a course of medical treatment. Complete control of the hyperthyroidism for a period of time, whether it be by thyroidectomy or by propylthiouracil, breaks the vicious circle of neuroendocrine disorders that are responsible for the maintenance of the hyperthyroid state.

Because it appears that complete control of the hyperthyroidism, for a period of several months or preferably from six months to a year, is a prerequisite for induction of a longstanding remission it is important to give a dose adequate to bring the basal metabolic rate to normal (0) or subnormal levels. Hyperthyroidism will recur promptly in those patients whose hyperthyroidism has been only partially controlled and also tends to recur promptly in those in which the period of control is unduly short.

McCullagh[1] has observed that 200 mg. of propylthiouracil will control the hyperthyroidism completely in 87 percent of the cases and 300 mg. will effect control in 96 percent. If hypothyroidism develops it is better to add small doses of thyroid than to reduce the dose of propylthiouracil to levels which may allow recurrence of hyperthyroidism. Small doses (10 mg. daily) of iodine given along with propylthiouracil do not significantly delay its action and may prevent the development of excessive vascularity. Propylthiouracil should be given in divided doses four times daily because the duration of the block induced by a single effective dose is short.[8]

The toxicity of propylthiouracil is low. No fatalities definitely attributable to its use have as yet been reported and agranulocytosis is rare. Side effects appear in about three percent of the cases and may be of sufficient severity to indicate discontinuation of treatment. Among the symptoms of toxicity are fever, skin rash, leukopenia, granulopenia, headache, and nausea. The incidence of agranulocytosis is so low that we have not believed it necessary to insist on weekly blood counts, but on merely checking the white blood count every two or three months when the basal metabolic rate is determined. We warn the patient to discontinue treatment and report at once for a blood count, if unusual symptoms should develop.

RESULTS OF TREATMENT

Experience in the treatment of over 300 patients by prolonged administration of propylthiouracil by Dr. E. P. McCullagh at the Cleveland Clinic indicates that it is difficult to obtain longstanding remissions in the following groups of cases.

1. Patients with severe hyperthyroidism (basal metabolic rate over +50) and large goiters (more than 2 or at most 3 times normal size). In these patients the hyperthyroidism tends to recur promptly as soon as medication is withdrawn or dosage decreased.

2. Patients who do not respond well to treatment and in whom a low grade residual hyperthyroidism persists despite the administration of the usual dose.

3. Patients with severe recurrent hyperthyroidism regardless of the size of the goiter.

4. Patients whose thyroids enlarge under treatment. In these cases not only does the hyperthyroidism tend to recur promptly when treatment is withdrawn but also the thyroid continues to enlarge so long as the drug is given.

5. Patients of a low order of intelligence or those who will not cooperate are poor subjects for prolonged treatment as they tend to discontinue treatment or take the medicine irregularly.

6. Hyperthyroidism associated with a nodular goiter may respond to treatment as well as Graves' disease, but patients with large nodular goiters often respond slowly and incompletely to ordinary doses. Since nothing but thyroidectomy removes the goiter and eliminates the remote possibility of a coexisting carcinoma, thyroidectomy after preparation with propylthiouracil is a more satisfactory method of treatment than prolonged medical treatment unless the patient's life expectancy be short and his condition poor.

The group of patients best suited for a trial of prolonged medical management in hopes of inducing a permanent remission, are those with small diffuse goiters and mild to moderate hyperthyroidism. Providing that the patient is willing and able to cooperate, providing that there is no intolerance to the drug, no enlargement of the thyroid during treatment, and provided that the response to 300 mg. of propylthiouracil daily is complete, there is about a 60 percent chance that the drug can be withdrawn after nine months of continuous treatment and that the remission will persist. In 20 percent of the cases, the hyperthyroidism will recur promptly and in the last 20 percent it will recur within a few months.

RADIOACTIVE IODINE

I^{131} is well adapted both physically and chemically to the treatment of hyperthyroidism. Since its half life is only eight days, nearly half of its radiation is expended in a week and most of it in a month. No detectable traces of radiation remain in the thyroid two or three months after treatment.

In hyperthyroidism I^{131} is concentrated in the thyroid exactly like the stable form of iodine, in concentrations up to 10,000 times as high as in any other tissue of the body. Thus the thyroid receives intense irradiation while other organs receive almost negligible amounts following the average dose.[9]

Since over 90 percent of the radiation of I^{131} is in the form of beta rays which penetrate the tissues for a distance of only one or two millimeters, there is no danger of serious injury to parathyroids, recurrent laryngeal nerve, trachea or other structures in the vicinity of the thyroid. Moreover since the I^{131} is taken up selectively by the parts of the thyroid that are functioning most actively, these areas are selectively inactivated without interfering with the potential function of areas that are inactive.

Since thyroid hormone contains iodine, and since in hyperthyroidism this hormone is fabricated in hyperfunctioning thyroid cells, it is theoretically possible to control the hyperthyroidism in 100 percent of the cases if sufficient I^{131} is given in divided treatments. In Graves' disease, when the uptake of I^{131} tends to be uniform throughout the diffuse hyperplastic goiter, one small dose usually suffices to effect a cure. In nodular goiter with hyperthyroidism, however, the uptake of I^{131} may be irregular and repeated doses may be required before the hyperthyroidism is controlled. By this technic the most active areas are first inactivated and then as the next most active areas take over the function they

in turn are inactivated by the second treatment and so on until a normal level of function is attained.

In a group of 28 patients all of whom have been followed longer than six months since the beginning of treatment, we have been able to control the hyperthyroidism in all cases.

In 19 patients with Graves' disease treated with I^{131} the average basal metabolic rate has fallen from +45 to 0. Control of the hyperthyroidism was effected by one treatment in over half of the cases and by two or three in the rest. The hyperthyroidism was well controlled in an average of three months after the first treatment. In most cases the thyroids are no longer palpable. Two patients have developed hypothyroidism.

In nine patients with nodular goiter with hyperthyroidism the average basal metabolic rate has fallen from +39 percent to +7 percent. The hyperthyroidism in all cases was well controlled in an average of five months after the first treatment. Two or three times as many treatments were required, however, and the total dose was three or four times as high. The average size of the thyroid has decreased from an estimated weight of 125 gms. to 70 gms. Hypothyroidism has not been observed.

The treatment of hyperthyroidism is to a large extent empiric whether it be by thyroidectomy, by propylthiouracil or by I^{131}. Surgeons have long known that a partial thyroidectomy for Graves' disease in which 5 gms. or more of thyroid is left often is followed by myxedema, whereas even the most radical subtotal thyroidectomy performed upon patients with normal thyroids or with nodular goiters causes no more than a transitory lowering of the basal metabolic rate. Similarly in Graves' disease a very radical thyroidectomy, in which only a few grams of thyroid tissue is left, may be followed by a recurrence of the hyperthyroidism. For these reasons we believe that attempts to estimate the exact amount of radiation that will be required to effect a desired result will often fail. Since the treatment of hyperthyroidism is essentially empiric it is safer to treat the patient by the method of Soley, giving repeated small doses until the desired effect is obtained.

In Graves' disease the required dose appears to be dependent more upon the severity of the hyperthyroidism than upon the size of the gland, although the latter must also be taken into account. Two or three mc. may control mild hyperthyroidism associated with small diffuse goiters whereas six to ten mg. may be required for very severe hyperthyroidism associated with large diffuse goiters. The average initial dose used in 80 percent of patients with Graves' disease is 4 mc. This dose may be repeated in two or three months if it proves inadequate or a smaller dose may be given if there is only slight residual hyperthyroidism. Since the full effects of the initial dose may not be apparent for four months, it is important not to treat the patient again too soon after the first dose if striking improvement has already been obtained.

In large multinodular goiters doses as high as 16 mc. may be given without danger of inducing hypothyroidism. The average dose is eight to 10 mc. repeated at two month intervals until the hyperthyroidism is controlled.

Occasionally a mild exacerbation of hyperthyroidism is observed in the first week or two following therapy, but aside from this no side effects or complications have been noted in 120 patients treated with I^{131}.

Although it is clear that I^{131} is a simple, effective and immediately safe method of treatment of hyperthyroidism, the ultimate results of such intense radiation are not yet known. The possibility of late carcinogenesis has been suggested, and for this reason I^{131} cannot be recommended for the treatment of younger patients without qualifications. Although there is as yet no clinical or experimental evidence that carcinoma of the thyroid can be induced by I^{131}, it is probably safer to limit its use to patients in the older age groups, or to those with recurrent hyperthyroidism or special problems of sufficient difficulty to justify the use of such intensive irradiation.

SUMMARY

At the present time there are three safe and effective means of treating hyperthyroidism: (1) thyroidectomy after preparation with propylthiouracil; (2) prolonged treat-

ment with propylthiouracil; and (3) administration of radioactive iodine.

Each of these methods is valuable in selected cases. The treatment of hyperthyroidism should be individualized and each patient should be treated by that method which assures the best prospect for a safe and definitive cure.

RIASSUNTO

L'ipertiroidismo puo' essere curato bene con tre diversi metodi:

1) tiroidectomia, dopo un'adeguata preparazione con propiltiouracile.

2) prolungata somministrazione di propiltiouracile.

3) somministrazione di iodio radioattivo.

La cura dell'ipertiroidismo va selezionata, nel senso che i pazienti dovrebbero essere affidati—in base alle condizioni individuali—a questo o a quel metodo di cura a seconda delle migliori prospettive di successo.

SUMARIO

Al presente poseemos tres metodos de tratamiento del hipertiroidismo: (1) la tiroidectomia previa preparacion por la propiltiouracil; (2) El tratamiento medico prolongado con la propiltiouracil; y (3) la administracion del yodo radioactivo. Cada uno de estos metodos es de valor en casos seleccionados; por lo tanto el tratamiento dela tirotoxicosis debe de ser individualizado y el metodo de seleccion debe de ser el metodo que ofresca mayores ventajas para cada paciente.

SOMMAIRE

Nous possèdons trois méthodes sûres et efficaces pour le traitement de l'hyperthyroïdisme.

1. Thyroïdectomie après préparation préoperatoire avec la propylthiouracile.

2. Traitement prolongé avec la propylthiouracile.

3. Administration de iode radio-activé.

Dans les cas sélectionnés, chacune de ces méthodes a de la valeur. le traitement de l'hyperthyroïdisme doit être individualisé et chaque malade doit être traité par la méthode qui est la plus apte de lui assurer une guérison sûre et définitive.

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Malignancy of the Thyroid Gland*

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MALIGNANCY of the thyroid gland is largely a preventable disease. Over 90 percent of all neoplasms of the thyroid arise in pre-existing adenomatous goiters.

Unlike malignancy in so many other organs, it is possible to prevent its occurrence in the thyroid. Prophylaxis may begin even before the birth of the child. All pregnant women residing in endemic goiter regions should receive a 10 mg. dose of iodine once a week, unless some form of goiter is already present. Likewise, all children in these areas should be given a similar amount of iodine until they reach maturity. If such a program could be successfully carried out, colloid goiters would be largely eliminated. Since adenomatous goiters develop in neglected colloid goiters as a matter of compensatory hypertrophy, these nodular growths would in turn be prevented, and malignant thyroids would largely cease to occur.

This undoubtedly is more than we can hope to do in the way of prevention, and yet it is not a Utopian idea. In Wisconsin we have had a goiter prevention program in effect under the joint supervision of the State Board of Health and the State Medical Society for the past 15 years. A recent survey revealed that approximately one out of every two children of school age in the state, or 240,000 children, are receiving iodine tablets once a week during the school year. Surveys have also shown a decrease in the incidence of colloid goiters from as high as 80 percent down to 10 percent.

While admittedly this preventive campaign is conceived on a long time basis, unquestionably results are being obtained, and not only colloid but also adenomatous goiters are gradually being eliminated. As chairman of this committee for the prevention of goiter in Wisconsin during this 15 year period, it has been personally gratifying to see a successful campaign progress against this type of cancer. Encouraged by our results in Wisconsin, I have recently appointed a committee of members of the American Goiter Assn. to study this problem on a national basis. Heading the committee are: Dr. Samuel Haines, thyroid authority, Mayo Clinic; and Dr. George Curtis, Ohio State University Medical School, whose studies on iodine in relation to the thyroid gland have been so valuable.

Cancer of the thyroid gland then is largely a preventable disease since the great majority of cases arise in pre-existing adenomatous goiters. There is nothing new or startling about this statement which has been accepted as a fact for many years. What is new is the fact that cancer of the thyroid is apparently increasing, that it is especially prone to occur in men having adenomatous goiters, and that not infrequently it may develop in children. These facts are new in the sense that we have come to recognize them in the past few years as a result of studies by various investigators.

As a consequence of these investigations and from a study of my own cases, I have now deviated from a 25 year policy and am advocating the removal of all adenomatous goiters in persons between the ages of 15 and 25. In the past I have advised parents whose child had an adenomatous goiter to leave it alone until the child was matured because of the possibility of a recurrence developing if surgery was performed before that time. Henceforth, I intend to advise operation when the child is 15 years of age or older despite this possibility because of the possible danger of cancer. Cancer in children with goiters is being reported by numerous writers.

Thyroid cancer in the male sex is no longer an uncommon disease and, like cancer of the lung, once we began to search for it we found it with increasing frequency. In my own series of 40 cases that I have just reviewed, there were 14 cases in the male sex.

The actual incidence of cancer of the thyroid in nodular goiter is a debatable question at the present time. Early writers on this subject

* From the Frieda Meyers Nishan Foundation for the Study of Goiter of the Jackson Clinic, Madison, Wis.

from the time of Kocher, Wilson, Graham, Mayo, Crile, and Pemberton have reported an incidence approximating four percent. In 1945 Cole stimulated great interest in this subject when he reported a startling figure of 17 percent. In a study of 192 nodular goiters, he reported that in 100 goiters of the multiple type cancer was present in 11 percent, and that in 92 of the solitary type it occurred in 24 percent. While these are considerably higher than those reported by other investigators, Cole's report served the valuable purpose of stimulating interest in this subject.

It has been my impression that cancer of the thyroid is becoming more prevalent, and a review of my cases showed five out of every 100 nodular goiters observed in the past five years to be malignant. Whether or not this is an actual increase, or whether it is due to the fact we are all becoming more cancer conscious and making a more careful search for malignant lesions, is a question.

It is a fact that for many years there was little interest in this subject despite occasional excellent articles in the literature. Certainly the problem was carefully considered by such authors as Kocher, De Quervain, Crotti, Joll, Dunhill, Eberts, Mayo, Crile, Graham, Lahey, Clute, Pemberton, Catell, Dinsmore, Hertzler, Means, Black, Tinker, Wilson, Kluick, and Davison, to mention only a few. Yet a resumé of the *Transactions of the American Goiter Assn.* showed few discussions upon this subject until the 1938 meeting when Pemberton reported a review of 774 cases seen at the Mayo Clinic.

Pemberton illustrated that cancer of the thyroid was not as hopeless a disease as it had been generally considered and that even cases that were recognizable clinically might be kept alive for many years. In particular, he stressed the point that in 60 percent of the cases operated upon, a diagnosis had not been made prior to surgery. That was likewise true in my own study, 18 of the 40 cases being unsuspected prior to thyroidectomy. This emphasizes the importance of removing all adenomatous goiters, since there are no clinical symptoms whereby the disease may be recognized in its early stages.

When a patient comes in stating that there has been a recent rapid growth of a long standing goiter, that there is hoarseness, shortness of breath, and a sense of constriction, it is probable that a neoplasm has developed and surgery is hopeless. I can see no reason why any physician should advise a patient not to have a nodular goiter removed. When one stops to consider that one out of every two of these tumors may in time become toxic, that 20 percent become substernal or intrathoracic and seriously interfere with respiration and embarrass the heart, and that one out of five may become malignant, there can appear no logical reason why they should not be removed when first recognized.

If tumors of equivalent size are diagnosed in other organs of the body, little time is lost in seeing that they are removed. Because goiters are commonplace, they are treated with too little concern by the laity and profession alike. In the hands of a competent thyroid surgeon the risk of either complications or mortality in a thyroidectomy performed for a nontoxic nodular goiter is negligible.

While it is true that approximately 90 percent of malignant goiters arise in pre-existing nodular growths, there are few rare lesions that do not arise as such. Pemberton and Black have shown that cancer of the thyroid does arise in the presence of exophthalmic goiter in which no demonstrable microscopic evidence of adenomatous tissue has been observed. The question of sarcoma of the thyroid is one concerning which there has been disagreement, some authorities even disputing the existence of this lesion. In my series, three apparent cases of typical sarcomata were seen.

A review of the literature regarding the pathologic classification of malignancy of the thyroid only serves to confuse the reader. It is not a matter of major importance so long as one recognizes the degree of malignancy and the chance of cure or at least of arresting the disease. Certain of the papillary adenocarcinomata are of a low grade type and, if thoroughly eradicated and followed with proper x-ray therapy, offer hope of possible cure. These growths are apt to occur in young people and comprise at least a third of all cancer of the thyroid. In this group are the so-called lateral aberrant thyroid tumors which at one time were believed to be malignant growths arising in congenital bits of

thyroid tissue located in the cervical gland region of the neck. Through the studies of Eberts, Clay, Wathuell, Pemberton, Black and others, we know now that these are actually metastatic lesions from the thyroid gland. If they are removed and if a total lobectomy is performed on the adjacent lobe and a subtotal lobectomy on the other lobe, there is a good chance of long survival.

Likewise, in many of the small adenocarcinomata, not observed by the surgeon but first detected by the pathologist, there is hope of cure. On the other hand, the diffuse adenocarcinoma is usually of short duration, grows rapidly, is highly malignant, and is seldom amenable to either surgery or roentgenotherapy.

Finally we come down to our newest form of therapy, radioactive iodine. For a time this seemed to offer great hope in treating those patients who could not be handled by other means at our disposal. To date, however, the results have proved unsatisfactory, and it seems probable that no case has yet been cured by this method. Unfortunately, only certain areas of the cancer are affected by radioactive iodine, so that at present this form of therapy is of little value. It is possible that further research along this line will lead to the development of a more successful agent.

In conclusion, I would like to emphasize that the thyroid gland offers a better opportunity for the prevention of cancer than any other organ of the body. Prevent the development of colloid goiter, and, in turn, eliminate most adenomatous goiters. Remove all adenomatous goiters when they are recognized between the ages of 15 and 25, and prevent the development of nine out of every 10 malignancies of the thyroid.

SUMMARY

Malignancy of the thyroid gland is largely a preventable disease. All children and all pregnant women residing in the endemic goiter areas should receive 10 mg. of iodine weekly. Prevention of colloid goiters will largely eliminate adenomatous goiters. Since nine out of every 10 neoplasms of the thyroid arise in pre-existing adenomata, eradication of the latter will largely eliminate cancer of the thyroid.

Adenomatous goiters should be removed on recognition, unless there is some special contraindication, and preferably in persons between the ages of 15 and 25. Conclusions based upon a study of 40 cases of cancer of the thyroid are presented. The high incidence of carcinoma of the thyroid in men and the high incidence in the solitary type of nodular goiter are emphasized.

RIASSUNTO

I tumori maligni della tiroide possono essere spesso prevenuti. Tutti i bambini e tutte le donne gravide appartenenti a zone nelle quali il gozzo e' endemico dovrebbero ricevere 10 mg. di iodio al giorno. Questa e' la prima fase di prevenzione, poiche' la prevenzione dei gozzi colloidi elimina a sua volta i gozzi adenomatosi. E poiche' sopra 10 tumori della tiroide, 9 originano da preesistenti adenomi, l'eliminazione di questi rappresenta la migliore cura profilattica dei cancri. Appena riconosciuti, i gozzi adenomatosi dovrebbero essere—a meno che non esistano speciali controindicazioni—asportati: cio' specialmente negli individui fra 15 e 25 anni.

L'A. richiama infine l'attenzione sopra l'alta incidenza di cancri della tiroide negli uomini e piu' specialmente nel tipo solitario dei gozzi nodulari.

SUMARIO

Las degeneraciones malignas de la glandula tiroidea son en general prevenibles. Toda criatura y toda mujer embarazada que habitan en regiones goitreogenicas endemicas deben de recibir 10 mgms de iodo por semana. La prevencion de los estrumas coloidales generalmente eliminan los estrumas adenomatosos. de cada dies caso de cancer del tiroides nueve ocurren en adenomas pre-existentes; por lo tanto, estos casos se pueden eliminar evitando los adenomas. Los adenomas del tiroides deben de resectarse tan pronto son diagnosticados especialmente en pacientes en las etapas de la vida de 15 a los 25 anos a no ser que existan contraindicaciones especiales. Se presentan las conclusiones del autor basadas en una serie de 40 casos de cancer del tiroides y la incidencia alta del cancer en el hombre asi como del tipo solitario nodular.

SOMMAIRE

Les tumeurs malignes de la glande thyroïde peuvent en grande partie être eviteés. Tous les enfants et toutes les femmes enceintes demeurant dans une région où le goître est endémique doivent recevoir 10 mg. d'iode chaque semaine; le prévention du goître Colloïde éliminera 9 des 10 neóplasmes de la glande thyroïde se developpant an adénome en grande partie les goîtres adénomateux. Vu que 9 sur 10 neóplasmes ont leur origine dans des adénomes préexistants, une éradication de ces derniers éliminera en grande partie le cancer de la thyroïde. Le goître adénomateux devra être enlevé aussitôt que diagnostiqué chez les personnes de 15 a 25 ans, à moins de contre-indication speciale. Ces conclusions sont basées sur une étude de quarante cas de cancers de la glande thyroïde.

L'auteur attire l'attention sur la fréquence du carcinome de la glande thyroïde chez l'homme et aussi sur la haute fréquence du goître nodulaire solitaire.

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Thyrotoxicosis Without Elevated Basal Metabolism*

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MANY believe that thyrotoxicosis and hyperthyroidism are synonymous terms and that clinical manifestations of a toxic goiter result from an excess of the thyroid hormone. Excess thyroxine produces elevated metabolism, weight loss, increased heart rate, often exophthalmos and other symptoms that typify toxic goiter. Many patients with goiter symptoms, however, do not fit into this category.

Patients with the type of thyrotoxicosis described in the previous paragraph show a definite pathological picture when the goiter is examined microscopically. The cells lining the acini show definite growth activity. Instead of the low cuboidal cells of the normal gland, they are columnar and proliferative, often piling up and producing buds that encroach on the colloid and tending to fill the acini.

There is another clinical picture often occurring in patients with long standing goiter in which the symptoms are predominantly cardiac. These patients may lack many of the symptoms of active thyrotoxicosis. They often have auricular fibrillation and all stages of congestive heart failure, from just edema of the lower extremities and moist rales in the bases of their lungs to free fluid in the chest cavities. They may have extreme dyspnea on exertion often with some cyanosis. They may

TABLE 1

Thyrotoxicosis without Elevated Metabolic Rate
—100 Cases

Age	Duration Goiter	Duration Symptoms	Weight loss	Pulse rate	B.M.R.
43.3	8.7[1] yrs.	2.3[2] yrs.	11.6[3] lbs.	102	+10

1—Nodular 10.6 years; diffuse 4.5 years.

2—Nodular 3.5 years; diffuse 2.7 years.

3—Nodular 63% lost weight; diffuse 97% lost weight.

TABLE 2

Duration of Goiter
Nodular (70)
Average duration 10.6 years

duration—years										
20 and over		2		3		3		3		11	
15 to 20		1	31%		20%		22%		50%	1	27%
10 to 15	1	2		2		1		1		7	
5 to 10		3	44%	6	48%	2	17%	2		13	19%
2 to 5		4		6		1				11	31%
2	1	3	23%			5	61%	2		11	
1 or less	1	1		8	32%	6				16	23%
Totals	3	16		25		18		8		70	
Age group	20 to 29	30 to 39		40 to 49		50 to 59		60 to 72		All ages	

* From the Hertzler Clinic, Halstead, Kans.

have a normal slightly elevated or even a subnormal basal metabolic rate. The nervous symptoms are often absent. The notable feature is the patient's facial expression, usually one of apathy and weariness. The outstanding pathological feature in the microscopic section of the glands of these patients is the presence of varying degrees of degeneration and the absence of hyperplasia. There may be nodules degenerated to the extent of being cystic and there is often present areas of replacement fibrosis. In areas where degeneration has not taken place, the acini are often large and lined with a single layer of almost squamous cells which certainly could not be interpreted as being active.

In the study of these glands many sections were taken from areas which grossly did not show degeneration and in none was cellular hyperplasia noted. T. C. Davison, Atlanta, Ga., long ago called attention to this type of goiter and called it "chronic hyperthyroidism with low basal metabolic rate." In the present state of our knowledge it would seem that we should regard this type of thyrotoxicosis as one resulting from an altered thyroid secretion rather than from an excess of the normal secretion.

The material presented in this paper represents a study of 100 selected goiter patients. A total of 700 were admitted for thyroid surgery during the two year period; 242 of the 700 had clinical evidence of toxic goiter with basal metabolic rates within normal limits. Four criteria were required to place a patient in the group of goiter patients.

The four points listed under "criteria" were chosen arbitrarily to eliminate equivocal subjects. The first requirement eliminated 56 patients. In addition, 37 patients qualified under the first three requirements but were eliminated because the admission pulse rate was under 88 per minute. Another 49 patients were eliminated because of original typing. This leaves 100 patients who fulfilled all of the following requirements.

Thyrotoxicosis without elevated metabolic rate criteria:

1. No iodine therapy during preceding six months.
2. Clinical evidence and symptoms of toxic goiter.
3. Basal metabolic rate plus 24 or less.
4. Resting pulse rate 88 per minute or over.

Table 1 shows composite average on the group of 100 patients. It includes 70 cases of nodular goiter and 30 with diffuse goiter. Thus the average patient is 43.3 years old, has

TABLE 3

Duration of Goiter
Diffuse (30)
Average duration 4.5 years

duration—years	20 to 29	30 to 39	40 to 49	50 to 59	60 to 72	All ages	
20 and over		1		1	1	3	
15 to 20	1					1	23%
10 to 15		1		1		2	
5 to 10		1				1	
2 to 5	1					1	
2	2		3			5	72%
1 or less	6	5	5	1		17	
Totals	10	8	8	3	1	30	

TABLE 4

Duration of Symptoms
Nodular
Average duration 3.5 years

duration—years							
Over 10		2	2	3	1	8	
5 to 10	1	3 (31%)	3 (21%)	2 (28%)	3 (50%)	12 (29%)	
2 to 5		5	4	7	2	18	26%
1 to 2	1	3	5	3	1	14	
½ to 1	2	1	4		1	7	26%
Under ½		2	6	3		11	
Totals	4	16	24	18	8	70	
Age group	20 to 29	30 to 39	40 to 49	50 to 59	60 to 72	All ages	

known of goiter eight and seven-tenths years, has experienced symptoms attributable to toxicity for three and three-tenths years and has lost 11.6 lbs. since the onset of symptoms. The resting pulse rate was 102 per minute. The basal metabolic rate was plus 10 usually the day following admission.

In a group of 100 one would expect many variations from the mean. For this reason it is desirable to analyze the picture from a different angle. For example, nodular goiter occurred more frequently in the older age groups (average age 45.5 against 38.2 for diffuse goiter). They had known of their goiters longer (10.6 years for the nodular against 4.5 years for diffuse). Sixty-three percent of the patients with nodular goiters had weight loss; 97 percent of the patients with diffuse goiter had lost weight.

Here we have arranged 70 cases of nodular goiter by age groups of the patients according to duration of the goiter (Table 2). The in-

TABLE 5

Duration of Symptoms
Diffuse
Average duration 2.7 years

duration—years							
Over 10				1		1	13%
5 to 10		1		2		3	
2 to 5	5	3	1	2	1	12	53%
1 to 2	1	2	1			4	
½ to 1	1	2	1			4	
Under ½	3	1	1	1		6	
Totals	10	9	4	6	1	30	
Age groups	20 to 29	30 to 39	40 to 49	50 to 59	60 to 72	All ages	

cidence is highest in the 40 year old group with numbers approximately equal in the preceding and following decade. One patient in the twenties had known of the goiter since 10 years old. For the group, 27 percent had had goiters for 10 or more years (11 percent for 20 years or over).

Diffuse goiter is more acute than nodular, probably on a quantitative rather than qualitative basis (Table 3). It is to be noted that it is by no means necessarily a disorder of young patients, though one-third of the series were under 30 years of age. More than one-half of the patients between 20 and 50 had noticed their goiters for a year or less. Twenty-three percent of the series had had goiters for five years or over.

An average duration of symptoms for three and one-half years gives no idea of the variation in a group of 70 nodular goiters (Table 4). Here one sees the wide distribution of duration versus age, with a fairly even spread throughout the table.

The distribution of symptom duration versus age is less evenly spread in diffuse goiter (Table 5). Here it is to be noted that patients under 50 years of age have had their symptoms for a relatively shorter period than the older age groups. Half of the entire group had had symptoms for two or more years.

The average pulse rate of 102 results from combining a rate of 88 to 96 in 43 patients with much higher rates in the remaining subjects (Table 6). In 57 patients the pulse rate was 100 or over. Twenty-six percent of the series had a pulse rate of 112 or over while five percent gave counts of 120 or over. The fairly even distribution over the table indicates no significant correlation between age and pulse rate.

Comparison of B.M.R. and age reveals no significant correlation (Table 7). Seventy-eight percent of the group had B.M.R.s entirely within normal limits; the remaining 22 percent cannot be considered as having significantly elevated B.M.R. For this reason no attempt was made to correlate the B.M.R. with duration of the goiter or with the heart rate.

Chemical analysis of thyroglobulin from toxic goiters after iodine therapy reveals alterations in the distribution of organic iodine. Chemical changes in goiter are:

1. Colloid goiters differ from normal colloid in: a. Decrease in total iodine; b. Decrease in thyroxine iodine; c. Increase in organic iodine in form other than thyroxine.

2. Most clinically toxic diffuse hyperplastic goiters have lowest thyroxine content.

3. Lowest thyroxine values found in goiters of long duration in old cardiotoxic goiter.

As shown in the graph (Chart I), normal thyroglobulin contains four-tenths percent total iodine. Ninety-three percent of this is present in organic form (iodoprotein). Roughly one-half of this organic iodine exists in the form of thyroxine.

TABLE 6

Pulse Rate
Nodular and Diffuse
Average 102 per minute

rate per minute	20 to 29	30 to 39	40 to 49	50 to 59	60 to 72	All ages	
Over 120		2	1	2		5	
112 to 120	3	4	8	5	1	21	57%
100 to 108	3	10	6	10	2	31	
88 to 96	7	9	14	7	6	43	
Totals	13	25	29	24	9	100	
Age group							

TABLE 7

Basal Metabolic Rate
Nodular and Diffuse
Average +10

B.M.R.	+20 to +24		5	6	3	8	22
	+10 to +19	5	6	8	11	1	31
	+1 to +9	8	7	10	5	1	31 78%
	−5 to 0	1	5	4	5	1	16
Totals		14	23	28	24	11	100
Age groups		20 to 29	30 to 39	40 to 49	50 to 59	60 to 72	All ages

Thyroglobulin from goiters removed surgically show: 1. Decrease in total iodine; 2. Decrease in thyroxine iodine; and 3. Increase in the nonthyroxine organic iodine fraction. All of the patients had received Lugol's solution before operation. This indicates that the goiterous gland is deficient in two respects: it is incapable of storing normal amounts of iodine; and it cannot convert organic iodine into thyroxine and store it in normal amounts.

Extracts from goiters contain a principle which stimulates the heart rate of thyroidectomized rats without a corresponding increase in rate of oxygen consumption (Chart II).

Total removal of the thyroid from 60-day old rats resulted in retarded growth. At the end of one month there is a decrease in oxygen consumption of 40 percent and a decrease in heart rate from a normal of 300 beats per minute to about 150 beats.

Thyroxine feeding produces comparable rise in both oxygen consumption and heart rate. Twenty micrograms of thyroxine iodine for three days brings both to approximately normal at the end of five days.

Extract from goiters fed in a dosage that causes no appreciable rise in oxygen consumption (five micrograms thyroxine-iodine daily for three days) stimulated the heart rate to normal or above. These extracts contained greatly reduced concentrations or thryroxine-iodine with greatly increased amounts of organic iodine other than thyroxine. Thus the lower the thyroxine-iodine—the greater the quantity of extract fed. These experiments indicate that the nonthyroxine fraction of thyroglobulin contains a principle capable of stimulating the heart without a corresponding effect on metabolism.*

TABLE 8

Effect of Goiter Extract 21874 on Metabolism and Heart Rate of Thyroidectomized Rats

Rat No.	Mg. Oxygen per kilo per hour			Heart Rate		
	Before	After	% Change	Before	After	% Change
1.	1350	980	−27	160	300	+88
2.	1230	1095	−11	180	300	+67
3.	1500	1600	+7	156	300	+92
4.	1108	1000	−10	150	277	+85
5.	1082	1090	0	144	276	+92
6.	960	1030	+7	180	300	+67
7.	1050	1000	−5	160	300	+88
8.	1008	1095	+9	220	330	+50
9.	1100	1110	+1	176	360	+84
10.	880	1080	+23	240	360	+50

*Endocrinology, **31:** 684-688, No. 6, Dec. 1942.

CHART I. DISTRIBUTION OF ORGANIC IODINE IN GOITER

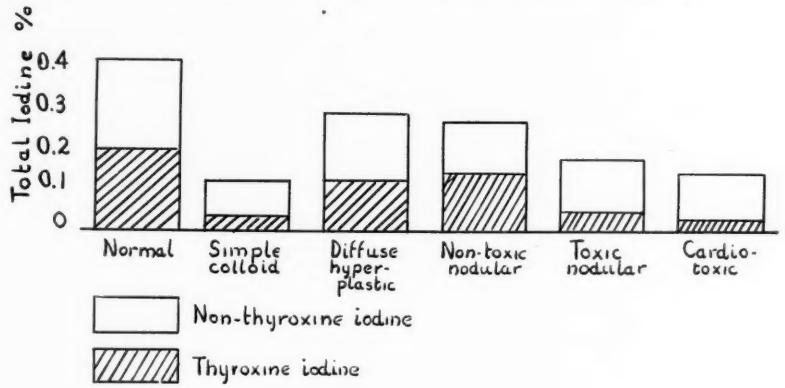
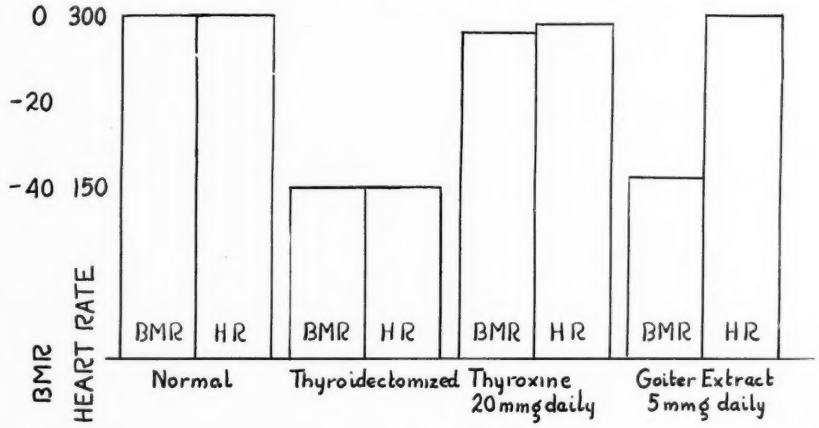


CHART II. CARDIAC STIMULATING PRINCIPLE FROM TOXIC GOITER EXTRACT (NOT THYROPINE)



CASE REPORT

Female, white, age 67, had had a goiter for 25 years. She also complained of tachycardia, palpitation and nervousness for one year. Her weight loss was 20 lbs. in one year. Hippuric acid was made, on admission, 58 percent; preoperative, 84 percent. The B.M.R. was plus eight; pulse and apex rate, 96; weight of the goiter, 194 gm. (Goiter extract 21874).

Chemical Assay: The total organic iodine was 0.12 percent (normal, 0.03 to 0.5 percent); thyroxine-iodine was eight percent (normal, 43 percent). The biological assay was made on young rats totally thyroideetomized at two months of age. Assays were made two months later, after oxygen consumption was stabilized at subnormal. Extract was administered daily by stomach tube for three days. Oxygen consumption and heart rate determinations were made before feeding, and again on the fifth day.

Dosage of Extract Fed: Over a three day period the dosage of extract given was 15 meg. of thyroxine-iodine per 100 gm. of rat. The total organic iodine intake was 180 meg. (165 meg. of nontoxic organic iodine).

Table 8 shows the effects of feeding experiments of this patient's goiter extract. Ten animals were used to minimize individual

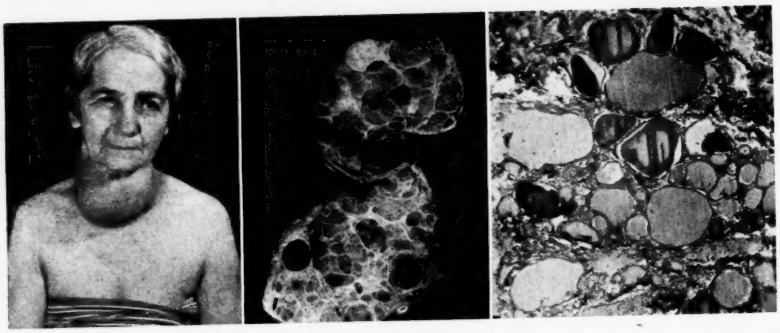


Fig. 1 (Case 1). Photograph of patient from whom goiter extract 21874 was made.
Fig. 2. Cross section of goiter from patient, showing degeneration and no hyperplasia.
Fig. 3. Photomicrograph of goiter in Figure 2, showing degeneration and no hyperplasia.

variations. On the left is the effect on goiter consumption, the average of which is relatively unchanged. On the right it is seen that increased heart rate resulted in every instance. All heart rates were determined by electrocardiographic tracings with the animals under light nembutal narcosis. We consider this as evidence that extracts from certain toxic goiters of long standing contain a principle which stimulates the heart rate of thyroidectomized rats without an associated increase in the rate of oxygen consumption.

SUMMARY

The concept that clinical manifestations of toxic goiter are due to an excessive production or liberation of thyroxine fails to explain thyrotoxicosis with little or no elevation of metabolic rate. It is felt that the term "hyperthyroidism" should be restricted to diffuse hyperplastic goiter in which elevated metabolism is an outstanding feature. The general clinical picture of thyrotoxicosis is best explained on the basis of perverted thyroid secretion instead of on the basis of excessive normal secretion.

RIASSUNTO

Il concetto che le manifestazioni cliniche del gozzo tossico siano dovute ad un'eccessiva produzione o liberazione di tiroxina non puo' spiegare i casi di tireotossicosi senza elevazione del ricambio basale. L'A. ritiene che il termine di ipertiroidismo vada riservato ai gozzi diffusamente iperplastici, nei quali l'aumento del ricambio basale sia l'esponente clinico predominante. Il quadro clinico della tireotossicosi e' spiegato meglio dal concetto di una pervertita, che non di un'eccessiva secrezione tiroidea.

SUMARIO

Segun el autor el concepto de hipersecrecion de la tiroxina en la produccion de las manifestaciones clinicas de la tirotoxicosis no explica esta condicion en aquellos casos que presentan un metabolismo normal o muy poco elevado. Por la tanto el termino "hipertiroidismo" se debe de restringir a los casos de hiperplasia difusa de la glandula con metabolismo elevado. En cambio el panorama clinico de la tirotoxicosis en general se explica mejor a base del distiroidismo o es decir de la perversion de la secrecion glandular.

SOMMAIRE

Les conceptions que la manifestation de goître toxique est dûe à une production excessive ou libération de thyroxine, n'expliquent pas pourquoi dans certains cas de thyrotoxicose, il y a pas ou presque pas d'élévation du métabolisme basal. L'auteur pense qu'on devrait restreindre le terme "hyperthyroïdisme." On devrait restreindre un terme au goître hyperplastique diffus dans lequel l'élévation du métabolisme est très évidente. Les symptômes de la thyrotoxicose sont mieux expliqués sur la base d'une secrétion thyroïdique pervertie que sur la base d'une secrétion excessive.

The Relation of Metabolism to Thyroid Surgery

MERRILL N. FOOTE, M.D., F.A.C.S.
BROOKLYN, N. Y.

EVEN today too many patients are being subjected to needless thyroid surgery because of an elevated metabolic reading. It is therefore timely to briefly evaluate this problem. The basal metabolic rate measures the calories per square meter per hour.

The surgeon, upon whose judgment rests the final decision as to whether or not an operation should be done for hyperthyroidism, should be a little familiar with some of the fundamental facts concerning the normal basal metabolic phenomena as well as its variabilities. "The Variability of Basal Metabolism," by Boothby, Berkson and Plummer, appeared in *Tr. of The Am. Assn. for the Study of Goiter*, 1937, and will be referred to at some length.

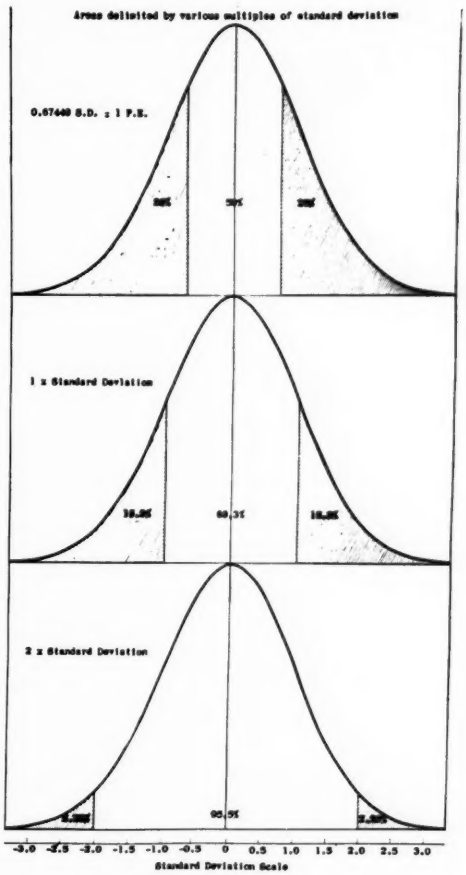
The normal or gaussian curve is "a symmetrical curve, in shape, and is completely defined mathematically for any given group by two constants, namely, the mean and the standard deviation. It is calculated as usual by adding all the observations, and by dividing the sum by the number of observations."

Boothby and co-authors during the period of 1917 to 1926 studied 7117 patients at the Mayo Clinic having non metabolic diseases and produced thereby the so-called "Mayo Foundation Normal Standards."

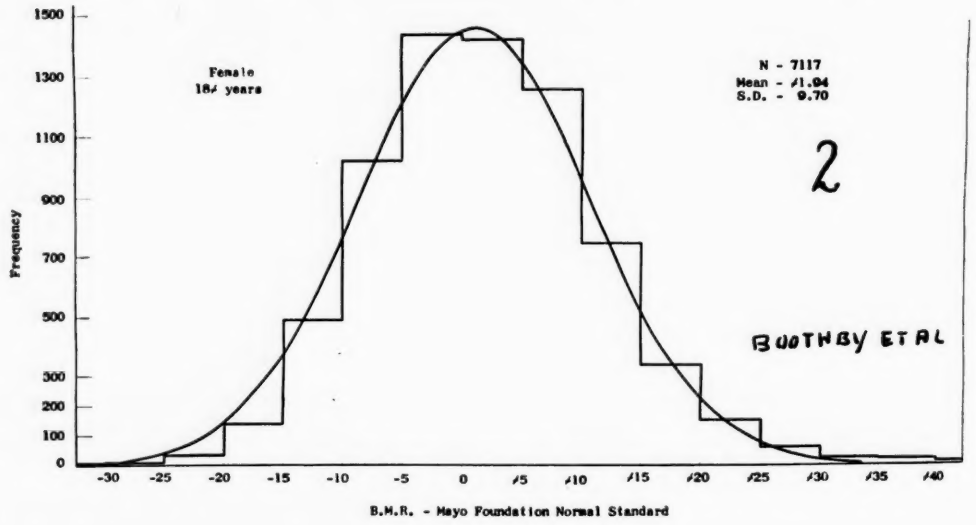
The results of the studies are represented in the figures 2, 3 and 4 and are self-explanatory. In conclusion Boothby states: "finally it must be recognized that basal metabolism as an actual observation, under any defined standard condition, is variable, like any biologic observation, and in consequence no one *lowest* metabolism has a prerogative to be considered *the* basal metabolism over any other measurements made under the defined conditions."

Every surgeon who does a large amount of thyroid work has a goodly number of cases constantly being sent to him for operation because of an increased basal metabolic rate. Upon careful evaluation however, many are not found to be suffering from hyperthyroidism, but from one of many other diseases or conditions in which an elevated basal metabolic rate is also found.

1

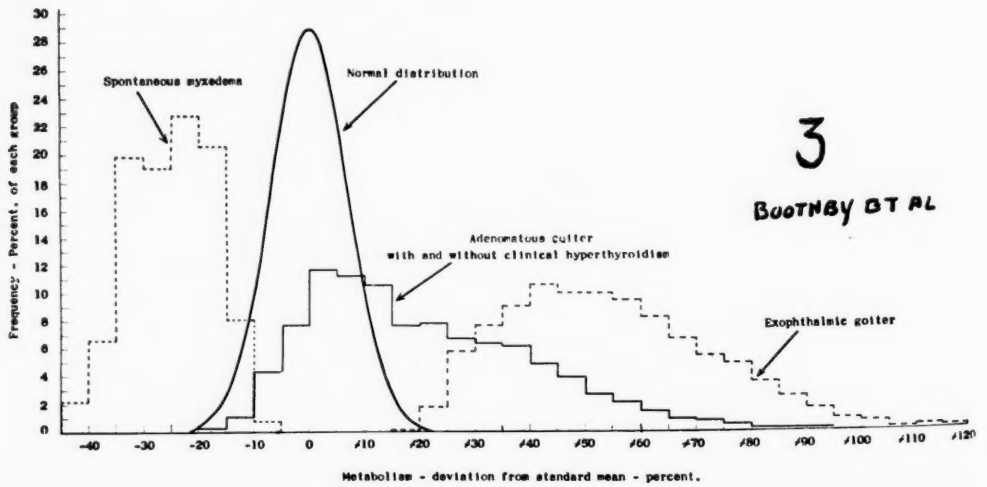

Areas delimited by various multiples of standard deviation
0.67449 S.D. = 1 P.E.
50%
1 x Standard Deviation
68.3%
2 x Standard Deviation
95.5%
-3.0 -2.5 -2.0 -1.5 -1.0 -0.5 0 0.5 1.0 1.5 2.0 2.5 3.0
Standard Deviation Scale

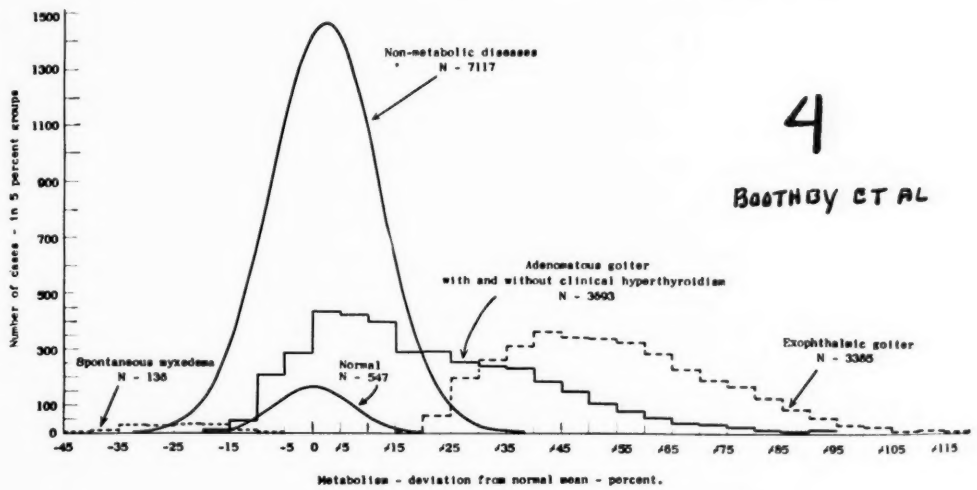
Normal or gaussian curve.
BOOTHBY ET AL



For many years hyperthyroidism was overlooked by the family physician and many patients were treated for some other non-existing disease. With the advent of the basal metabolic machine, which is now a part of the equipment in most doctors' offices, and with the literature replete with rules of thumb by which a diagnosis of hyperthyroidism can be easily made, and because of the satisfactory results of surgery properly done on properly selected cases, it is not difficult to understand the frequent errors that are therefore made, in diagnosing this condition.

It is true that most cases of hyperthyroidism are associated with elevated basal metabolic readings. Many elevated basal metabolic ratings, however, are not indicative of hyperthyroidism. There are several reasons for this. In the first place, numerous psychical, physiological and pathological processes, other than





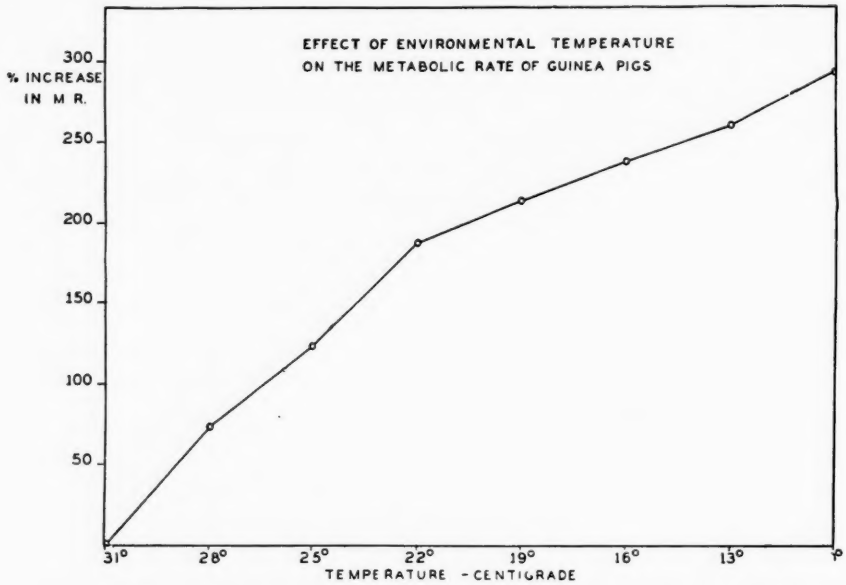
toxic goiter, are accompanied by an increased basal metabolic rate. Any condition which causes rapid respiration such as emotional states, or exercise, the menstrual cycle; diseases, such as cardiac disorders, tuberculosis, diabetes, various heart conditions, some malignancies, especially lymphosarcoma, or any disease accompanied by a fever will result in an increased basal metabolic rate. Other rather common diseases producing an increased metabolism are leukemia, anemia, and disorders of the pituitary and adrenal glands. Riddle has shown that the metabolism rate in pigeons which have received thyroid or thyrotropic hormone was increased when the basal metabolic reading was done at the critical temperature, but that it was decreased when the measurements were made at 15° centigrade. Collip and Billingsley confirmed these findings while experimenting with rats and guinea pigs.

The basal metabolic rates in children are notoriously unreliable. In the first place it is difficult to obtain a true reading in children; and when the reading is obtained it is very apt to be abnormally increased, without any evidence of hyperthyroidism being present. On the other hand, a persistently low basal metabolic reading is rarely present in cases of hyperthyroidism. It is necessary to base one's judgment largely upon clinical experience in dealing with hyperthyroidism in the younger age group.

In addition there are many mechanical and technical errors which may play a role in producing an increased consumption of oxygen; such as the inaccurate adjustment of the breathing tube in the patient's mouth, or the improper application of the clip on the nose, faulty flutter valves, leaking tubes, or an alteration of the chemical substances used in some of the metabolism machines. After all, the metabolism apparatus only records the amount of oxygen consumed by the patient per minute. This may, in no way be related to hyperthyroidism. As stated above, *the basal metabolic rate measures the calories per square meter per hour.*

Means has properly said that basal metabolic readings are "never too low unless the patient goes to sleep, or unless there is a technical error on an inward leak in the apparatus being used. All other errors which tend to make the test inaccurate (making it too high) are recent exercise, eating, emotional states, fever and etc. It is apparent then that a single low reading is more apt to be accurate than a single high reading."

Krogh has called attention to the fact that "adventitious departures from the usual basal conditions more frequently raise than lower the measured metabolism." It might, there-



Showing the effect of lowering the environmental temperature upon the metabolic rate of the guinea pig. Points on the curve represent an average of three determinations on a group of eleven pigs.

fore, have been better to use the term "standard metabolism" than basal metabolism.

Boothby has shown that in a group of normal individuals, "adult males are more variable in their metabolic readings than females. Repeated determinations for individual females are, however, more variable than for males. Therefore, when single determinations for many individuals are used to measure the variability, the total gives a larger net variability for females."

It seems fair to assume that the basal metabolic reading is only another laboratory test which should always be carefully considered but not necessarily considered too seriously. Basal metabolism readings will never replace the clinical judgment of the physician in charge or the surgeon to whom the patient is referred.

Repeated tests on the same individual either before or after operation, if done under as nearly similar conditions as is possible, are of great value in determining whether the metabolism is rising or falling. This test is helpful in following an individual case for a relatively long period of time. It is far more valuable in a situation of this sort than a single reading in making the diagnosis of hyperthyroidism.

Generally speaking the basal metabolic rate is more apt to reflect accurately the degree of toxicity in toxic diffuse goiters than it is in toxic nodular goiters. This is to be expected because the onset of toxic nodular goiter is far more insidious, and the clinical symptoms are definitely less severe than they are in toxic diffuse goiters.

Dr. T. C. Davison has called attention to a group of cases in which the signs of hyperthyroidism have been present over a long period of time. The patients are moderately toxic and manifest all of the clinical signs and symptoms of hyperthyroidism but the basal metabolic readings are consistently low. He has termed this entity "chronic hyperthyroidism." We have all been aware of this condi-

tion, and also of the fact that these patients, even though they do have signs of toxic goiter with a low metabolic reading, are relieved of their clinical symptoms after proper resection of the thyroid gland. It is interesting to note that operation does not decrease the basal metabolic rate in the same ratio as the signs of hyperthyroidism are decreased.

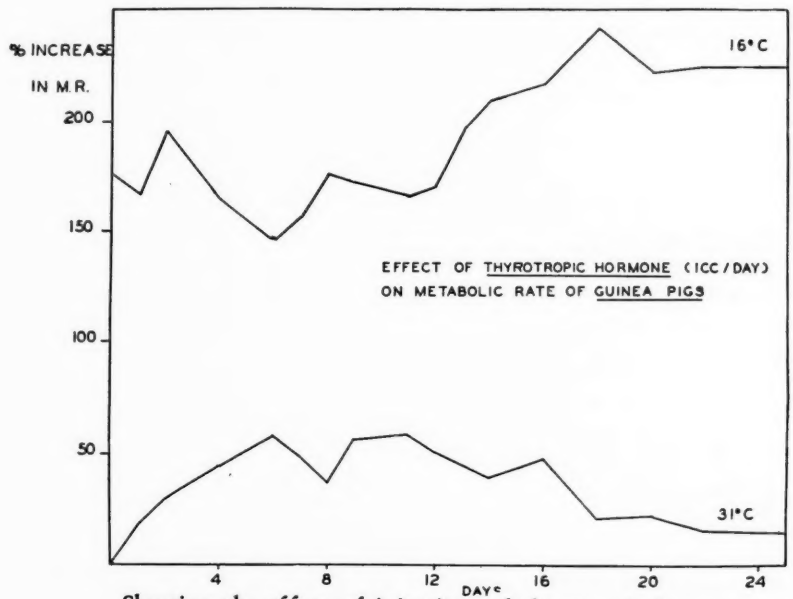
For years we have taught our residents that we are less impressed by a single metabolic reading in diagnosing toxic goiter, whether it be of the diffuse type or of the nodular type, than we are by the results of a careful history and a proper physical examination.

It should always be stressed that there is never any hurry about making a decision as far as surgery is concerned in any patient having a questionable toxic goiter. If the symptoms are so bizarre that they are difficult to interpret in terms of toxic goiter, prolonged study and observation are indicated.

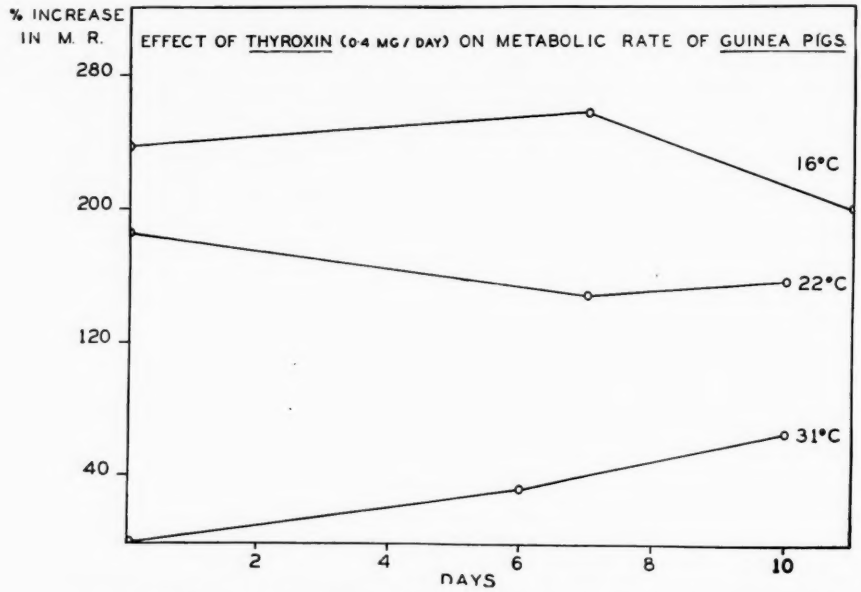
If research leads to the conclusion that the condition is not one of toxic goiter, an unnecessary operation has been avoided. The patient has not been made worse. The surgeon has been spared self-criticism.

The most important determination is whether or not the patient is suffering from hyperthyroidism. After this has been established, the degree of hyperthyroidism can then be carefully evaluated; and as a matter of fact the degree of hyperthyroidism, at the present time, makes very little difference anyway because, with the proper use of antithyroid drugs, almost any degree of hyperthyroidism can be controlled so that surgery may be done safely.

We do not want to give the impression that basal metabolic readings should not be done, and should not be given thoughtful consideration. They are of the utmost help in studying severely toxic diffuse goiter, or severely toxic adenomatous goiter and in determining the progress of the disease after the diagnosis has been made or after surgery has been done.



Showing the effect of injections of thyrotropic hormone on metabolic rate of the guinea pig measured at two temperatures 31°C. and 16°C. Points on curve represent average of determination on seven animals.



Showing the effect of injections of thyroxine upon the metabolic rate of the guinea pig measured at three temperatures, 31° C., 22° C. and 16° C. Points on the curve represent average of determinations on twelve animals.

We do believe, however, that an accurate daily recording of the body weight and the pulse rate, if done under similar conditions, is a valuable adjunct to the basal metabolic reading, and will usually give as reliable an indication of the metabolic status as does the reading itself.

If a patient with toxic hyperthyroidism is given Lugol's solution, and placed on a proper thyroid regime, and if the pulse rate tends to come down gradually but constantly, with weight tending to increase constantly, regardless of what the machine shows, the metabolism must be decreasing. By keeping a graph of the pulse rate, and the body weight, one is in a position to determine the optimum time for surgery, in spite of what the basal metabolic reading is. As soon as the weight ceases to increase, and as soon as the pulse ceases to decrease, at which time the metabolism will cease to drop, it is then time to operate even though, the metabolism cannot be brought to a normal level.

We have all had experience with the patient suffering from highly toxic goiter, accompanied by a high metabolic reading. This patient after careful preparation has been found to improve clinically as far as the weight, pulse curve and clinical symptoms are concerned, but in whom the basal metabolic rate still remains alarmingly high. Such a patient will usually respond to subtotal thyroidectomy with little or no reaction.

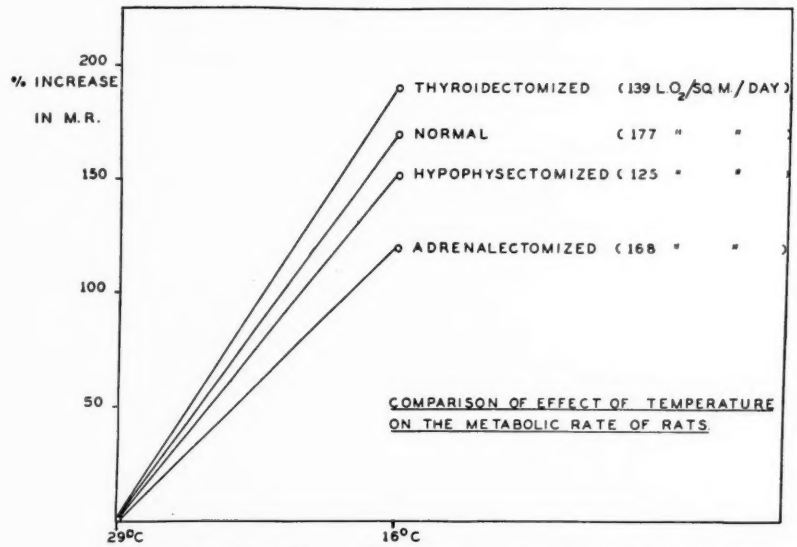
At the present time, with proper use of the antithyroid substances, if there are no untoward reactions to them, it is almost always possible to bring the metabolism to a normal or nearly normal reading if we persist in their use long enough. Of course, it is needless to state, that no patient who has been given propylthiouracil or any similar antithyroid substance should ever be operated upon until the gland has been involuted by the use of iodine.

It has been our experience that the cases with toxic nodular goiter respond favorably

to the preoperative use of iodine although not to the same degree as does toxic diffuse goiter. A certain number of them will not have their basal metabolic rates return to normal. In such cases we must determine whether or not it is wise to operate in spite of the basal metabolic reading. We find that most of these cases respond just as well to surgery as do those whose metabolism has returned to absolute normal.

and the accompanying symptoms disappear.

Unfortunately, in many patients suffering from the Froelich syndrome, the rate of the metabolic reading or the blood cholesterol do not always indicate the amount of thyroid needed to control the symptoms. This can only be determined by trial and close observation. If the symptoms are aggravated by the administration of thyroid, there is probably no hyperthyroidism present, and the continua-



Showing the effect of lowered environmental temperature upon the metabolic rates of thyroidectomized, normal, hypophysectomized and adrenalectomized rats. Values shown represent averages of determinations on groups of animals from eight to 33 in number.

There is a group of nonsurgical thyroid conditions which produce an elevation or a depression, as the case may be, of the basal metabolic rate. Some obese patients are found to have an increased metabolic rate, accompanied by tachycardia, nervousness and cardiac palpitation. High uric acid, high nonprotein nitrogen, polydipsia, polyphagia and an increased galactose tolerance tests are present. Many of these individuals have what has been termed thyroid-pituitary obesity. If thyroid extract and pituitrin are administered, the weight and the metabolic rate decrease,

tion of thyroid medication may cause very critical symptoms. One must then look for a pituitary or an adrenal insufficiency. If the administration of dessicated suprarenal is promptly followed by improvement, it may be assumed that the condition is one of hypoadrenia.

One is sometimes confronted by markedly undernourished patients having a low basal metabolic reading, and in whom there are no other signs of hypothyroidism. A low basal rate is frequently found in Addison's disease, lipoid nephrosis, and in malnutrition due to

starvation. These patients, like the obese, may be the subjects of adrenal or pituitary deficiency, or a combination of the two. They are made worse by taking thyroid extract. Not infrequently, however, proper doses of adrenal and pituitary substances will dramatically alleviate their symptoms.

The clinical reactions to heat and cold will often aid in differentially diagnosing hypothyroidism from adrenal or pituitary deficiency. In all three diseases, there is a marked intolerance to cold; but in the latter two, namely hypoadrenalism, and hypopituitarism, the symptoms are made worse by extreme heat, whereas in hypothyroidism heat is welcome and well tolerated.

Lerman and Stebbins have warned that extreme caution must be used in giving thyroid extract to patients with pituitary myxedema. Cases have been reported in which coma and death followed its administration. Thyroid may throw a patient with Addison's disease into acute adrenocortical failure.

Because of the bizarre, conflicting and overlapping symptomatology in Simmond's disease (atrophy of adrenals, thyroid, parathyroids, pituitary and ovaries) which may be made worse by thyroid medication, and because this condition may be mistaken for simple hypothyroidism, which usually responds to thyroid medication, it is again emphasized that its administration should be given with great care. Should pituitary myxedema be treated with thyroid, and should untoward symptoms develop, measures to protect adrenocortical failure and hypoglycemia must be instituted. It has been found that in adrenocortical failure the blood sodium and chloride are reduced while the chloride excretion is increased.

Wilder says that a sharp fall in blood sugar with a very gradual increase following the injection of insulin, suggests hypopituitarism, and it is found that the F.S.H. test in the urine is negative. The 17 ketosteroids in the urine are absent. However, these are also found to be absent in females suffering from Addison's disease. The blood cholesterol is low. The response to thyroid medication is unfavorable. Therefore, if average doses of thyroid are given, and are followed by abdominal cramps, anorexia, vomiting, asthenia and collapse, it must be assumed that the patient has pituitary myxedema and not thyroid myxedema. Should these symptoms develop, sodium chloride and fluids should be given intravenously, as well as Gonadgen, in order to protect the adrenals and thus prevent adrenocortical failure.

SUMMARY

1. The variabilities of metabolic rates in patients with nonmetabolic diseases have been mentioned.

2. Some of the conditions and diseases other than those of the thyroid gland which are associated with elevated basal metabolic readings have been discussed.

3. The unreliability of the basal metabolic rate in making the diagnosis of hyperthyroidism has been stressed.

4. The necessity of sound clinical judgment and experienced observation in making the diagnosis of hyperthyroidism has been emphasized.

5. Unnecessary operations which have been done only because of an increased basal metabolic rate without symptoms of clinical hyperthyroidism have been deprecated.

6. Some differences between pituitary myxedema and thyroid myxedema and the possible danger of giving thyroid medication to patients who may have myxedema due to conditions other than hypothyroidism have been stated.

RIASSUNTO

1. Ricorda le variazioni del ricambio basale in pazienti affetti da malattie non metaboliche.

2. Discute talune condizioni e talune malattie associate ad un elevato ricambio basale, senza la necessaria partecipazione della tiroide.

3. Sottolinea la scarsa attendibilita' del motabolismo basale quale metodo diagnostico per l'ipertiroidismo.

4. Richiama l'attenzione sopra la necessita' di una larga esperienza e di un accurato giudizio clinico per la diagnosi ipertiroidismo.

5. Espone la frequenza di operazioni non necessarie, intraprese solo in base ai risultati del ri cambio basale, trascurando piu' o meno completamente i sintomi clinici.

6. Differenzia il mixedema ipofisario dal mixedema tiroideo, accennando al pericolo di

somministrare estratti tiroidei a pazienti nei quali il mixedema non e' dovuto ad un effettivo ipotiroidismo.

SUMARIO

Se ha mencionado la variabilidad del metabolismo basal en pacientes con enfermedades no-metabolicas.

Se ha discutido las condiciones y las enfermedades que producen elevacion del metabolismo basal.

El metabolismo basal no es por lotanto criterio infalible en el diagnosis de la tirotoxicosis. El criterio clinico es el mas importante y este debe de tomar en consideracion la observacion experimentada de las manifestaciones que presente el paciente.

El autor critica las tiroidectomias innecesarias que se han practicado a base de la elevacion del metabolismo sin verdadera manifestaciones clinicas de hipertiroidismo.

El autor tambien discute la diferencia entre el mixedema de origen pituitario y tiroideo y los peligros del medicamento tiroideo en las mixedemas no-tiroideas.

SOMMAIRE

1. Les variations du métabolisme basal chez les malades ne souffrant d'aucune maladie métabolique sont mentionneés et discuteés.

2. Quelque unes des conditions et maladies autres que celles de la glande thyroïde, présentant une élévation du metabolisme basal sont discutées.

3. On ne doit pas se laser entièrement sur le taux du métabolisme normal, pour faire le diagnostique d'hyperthyroïdisme.

4. Il est nécessaire que le chirurgien possède un jugement clinique sérieux; il doit aussi avoir beaucoup d'expérience pour faire le diagnostique d'hyperthroïdisme.

5. Des opérations inutiles ont été faites parce qu'il y avait une hausse de métabolisme basal sans symptômes cliniques d'hyperthyroïdisme.

6. Il y a une difference entre le myxédème pituitaire et le myxédème thyroïde e un danger peut résulter de l'administration d'extrait de thyroïde aux malades qui ont un myxédème dû a des conditions autres que l'hyperthyroïdisme.

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Radioiodine in Thyroid Disease*

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INNOVATIONS in the recognition and management of thyroid disease are of stimulating interest. The discovery of artificially induced radioactivity by Joliot and Curie,[1] preceded by the earlier disclosure of radioactive substances by Becquerel and the Curies, gave to medicine a new and powerful technic. The building of the cyclotron by Lawrence and his associates made this technic practical.[2]

The use of radioactive isotopes for the purpose of "tagging" certain significant elements to be used as "tracers," is based upon their property of being essentially identical with their more common prototypes, yet bearing physical characteristics which may be readily followed. These isotopes, such as radioactive iodine, it was soon recognized, could be employed to study the course and ultimate fate in the body of ingested substances and their subsequent history of synthesis, absorption, distribution, endogenous metabolism and excretion. Prior to the use of radioactive isotopes, there was no known method for differentiating the iodine given during a particular experiment from that already present in the body. The use of radioiodine in the negligible quantities in which it could be employed, lent itself readily to a study of the fate of both administered and nutritional iodine.

In 1938 appeared the first publication concerning the use of radioiodine as an indicator of thyroid physiology, by Hertz and his associates.[3] At that time there was but one radioisotope of iodine available. This radioiodine (I_{128}) had a "half-life" of only 25 minutes, thus restricting the biologic studies to a necessarily brief period. During the year, the number of radioisotopes of iodine was increased to five. These were prepared by cyclotron bombardment of iodine, tellurium or antimony with neutrons, deutrons or helium ions.[4] The bombardment of metallic tellurium with deutrons gives rise to two forms of radioiodine, one with an atomic weight of 130 and a 12.5 hour "half-life," the other with an atomic weight of 131 and a "half-life" of eight days. This latter is experimentally the most valuable, and is now the most widely used clinically.

The demonstrable facts of thyroid physiology indicate that iodine is selectively taken up by the thyroid gland, further that in some measure glandular function is regulated by its iodine content. This is further substantiated by the radioiodine experiments, which demonstrate that iodine is selectively collected by the thyroid under normal conditions and in a definite measurable amount.

Studies with radioiodine soon substantiated the earlier more tedious chemical investigations in demonstrating the great preferential avidity of iodine for thyroid tissue in animals.[5-6-7-8] Far less administered radioiodine is collected by the other organs such as the spleen, liver, pituitary or the muscles.

It was soon found that the time required for the initial collection of iodine by the thyroid cells is determined mainly by the time required for the injected material to reach the thyroid gland.[5] Uptake of iodine by the thyroid is thus extremely rapid.[8] With the introduction of the tracer dose of radioiodine to follow the endogenous metabolism of iodine, Perlman *et al.* found that the thyroid removes iodine from the circulation much faster than it can come into equilibrium with the nonthyroid tissues, and that the subsequent release of radioiodine from the gland is much slower than its initial uptake.[9]

The radioiodine collected by the thyroid is influenced by the amount of iodine administered, previous iodine administration, the degree of thyroid stimulation or depression and the existence of thyroid disease. For normal thyroid glands, the per cent of iodine collected increases as the intake is decreased.[5-6-9] It is this relatively large percentage uptake from *small* injections which may account for

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the physiologic maintenance of normal thyroid function on the minute quantities of iodine usually found in the diet.[5] This rapidity of utilization of small amounts points toward the necessity of a regular iodine intake. The rat thyroid gland after being saturated with iodine, recovers its ability to fix iodine in a little more than three days.[6]

In 1938 and again in 1940 Hertz and his associates,[3-5] using radioiodine, showed that hyperplastic thyroids fix iodine more rapidly than normal glands. Rat thyroids, rendered hyperplastic by an iodine-deficient diet, acquire an increased ability to fix iodine.[10] The resultant thyroid and hypophyseal changes in these goitrous animals indicate an excessive release of thyrotropic factor from the pituitary.[10] Thyroids of hypophysectomized animals collect much less radioiodine than thyroids of intact animals, yet still exceed other body tissues in this ability.[6] On the other hand, thyroids of animals treated with thyrotropic hormone collect more radioiodine than the glands of normal controls.[6-11]

The next step in the development of further understanding of thyroid function was logically a study of the mechanism of iodine fixation and of hormone synthesis by the thyroid gland.

Iodine upon being absorbed by the thyroid gland enters into at least four separate phases:[12] 1. iodine ions in the thyroid follicular cells; 2. a bound iodine fraction known as "iodinase"; 3. diiodotyrosine and 4. thyroxine. When tracer iodide is first administered[12] it accumulates largely in the gland at phase one. Near the end of the experiment it will exist largely in phase four. The radioiodine does not appear uniformly distributed throughout all phases. Radioiodine studies soon demonstrated that iodine is quickly brought to the follicular cells by the blood stream and rapidly converted into diiodotyrosine and thyroxine; moreover, that within a matter of a few hours these organic iodine compounds may return again to the circulation.[9-13] With increasing time intervals subsequent to radioiodine administration, concentration is first demonstrable in the diiodotyrosine-like fraction; the longer the time interval, the more is found in the thyroxine-like fraction.[9-13] It was further demonstrated that the diiodotyrosine fraction appears to be the natural precursor of thyroxine.[14]

In addition to thyrotropic hormone[6-11] other substances may affect the ability of the thyroid cell to collect and fix radioiodine.[15] Administration of relatively large amounts of inorganic iodide blocks the subsequent formation of organic iodine in the thyroid gland.[16] This block is related to the level of the plasma iodine. When this is above 20 to 35 micrograms percent, there is no appreciable conversion of inorganic iodide to organic forms within the gland. Conversion of diiodotyrosine to thyroxine was considered slower when large amounts of iodide were injected.[16]

Further increase in the plasma iodine, probably by influencing the level of inorganic iodine in the gland, is an inhibitor of normal thyroid function.[17] This period of inhibition can be prolonged by preventing the escape of administered iodine through the excision of the kidney.[17] This inhibition of the organic-binding of iodine by the gland when the plasma iodine is kept high may be offered as a part of the mechanism of response of the hyperthyroid patient to iodine therapy.

In addition to the iodides there are other substances which can be demonstrated by the use of radioiodine to influence thyroid function. Some of these, cyanides and sulfides for example, as demonstrated by the amount of accumulation of radioiodine by thyroid slices, may act by hindering the collection of iodide.[18] Others, such as various sulfonamides,[18] and particularly thiouracil and its related compounds, may inhibit the formation of diiodotyrosine and thyroxine[19] without affecting the iodine concentrating power of the thyroid. Potassium thiocyanate not only depresses the chemical conversion of inorganic iodine by thyroid slices, but also prevents the collection of iodine.[19]

The administration of thiouracil depresses the uptake of radioiodine by the intact thyroid gland.[20] Recovery, as judged by the iodine concentration capacity of the thyroid, as well as the amounts of radiotyrosine and radiodiiodotyrosine formed, is complete two weeks after this goitrogen has been discontinued. The degree to which thiouracil and its allies prevents the formation of an iodinated hormone,[21] varies with the particular agent ad-

ministered and also with the animal species.

The iodine collecting capacity of thyroids made goitrous by means of various chemical agents, appears to be partly a function of the time elapsing after the last administration of the goitrogenic substance.[22] This is borne out by the administration of thiocyanate, which depresses the uptake of radioiodine only so long as high concentrations of the drug remain in the circulation.[22]

The goitrogenic effect of various foods may also be studied by observing the subsequent inhibition of radioiodine uptake. Of 61 different foods thus tested in 100 different subjects,[23] rutabagas were found to contain the greatest antithyroid activity. Vegetables were more active than animal products.

The use of radioisotopes has made possible the study of the metabolic fate of active drugs, such as thyroxine. When this hormone, tagged with radioiodine, is injected into rats, more than 50 percent of the administered dose may be recovered after two hours; in the gastrointestinal tract, liver and in the pancreas, mainly in an unaltered form.[24] The thyroxine appears to enter the intestinal tract by way of the liver. These results are clinically interesting because of the apparent relationship between thyroid and hepatic function.

The rate of conversion of injected radioactive inorganic iodine into protein-bound plasma iodine has been suggested as a useful guide to thyroid activity.[25] Urinary excretion is likewise of possible usefulness in making a differential diagnosis,[26-27-28] especially when routine methods are inapplicable, for example where the BMR is high due to nonthyroid factors.[26]

Keating and his associates found the urinary excretion of tracer doses of radioiodine less than normal in hyperthyroid patients.[28] McArthur *et al* demonstrated that a low urinary excretion of radioiodine is helpful in establishing a diagnosis of Graves' disease while a high excretion helps in excluding such a diagnosis.[27] Skanse and Riggs[29] using this technic, were thus able to diagnosis "*thyrotoxicosis factitia*" (self-induced thyrotoxicosis), since the urinary excretion of radioiodine was higher than normal.

Direct measurement of the iodine uptake by the thyroid has been suggested as an even more accurate method for demonstrating an index of thyroid function.[30] Werner and his associates[31] found the normal uptake to be 20-30 percent of the administered tracer dose of 50-75 microcuries. Anything more than 40 percent was regarded as definitely hyperthyroidism; anything less than 10 percent, as hypothyroidism.

The concentration of radioisotopes which can be fixed and maintained in various types of tissue, fluctuates widely.[12] Several factors are involved in the turnover rate, such as the natural avidity for iodine, the stage of the disease, differentiation of the tissue and topographical variations of the specimen.

Employing the radioautographic technic, Leblond demonstrated that most of the radioiodine, administered in varying doses, was deposited in the colloid rather than in the cells.[32] A similar preferential distribution was shown in pituitary-treated and in hypophysectomized animals.

In our clinic, studies of the goiters of two patients who had received radioiodine prior to thyroidectomy; one a diffuse colloid goiter and the other a diffuse hyperplastic goiter with hyperthyroidism (exophthalmic goiter), also showed a preferential distribution in the colloid.[33] Hamilton *et al.*, employing the autographic method, found that in goitrous glands radioiodine was in general concentrated in the most actively functioning parts of the goiter.[34]

Further studies in our laboratories, of the fate of radioiodine in six nodular goiters showed that nodular formation and particularly one nodule of a fetal adenomatous type, were less active than the surrounding thyroid tissue.[35] The histologic pictures of the nodules of the six nodular goiters showed wide variations. The nodules of the patients with toxic nodular as well as of exophthalmic goiter were of the hyperplasia-involution type (not "true adenomas"). All nodules showed a decreased function as compared to the corresponding paranodular thyroid tissues. This was demonstrated by a smaller iodine content in the nodules, a lesser iodine fixation and a slower turnover of iodine.[35a] Moreover, the formation of thyroxine was comparatively minimal in the nodular tissue.

The nodules of patients with nontoxic nodular goiter, toxic nodular goiter and the so-

called fetal adenoma studied appeared functionally autonomous.[35b] They showed less avidity for administered radioiodine and also much less thyroxine and diiodotyrosine production than the surrounding thyroid tissue.

The diffuse goitrous tissue of two patients with nontoxic diffuse colloid goiter[35b] showed a great avidity for iodine, but its ability to produce thyroxine and diiodotyrosine did not appear increased. The diffuse hyperplastic tissue of a patient with exophthalmic goiter showed the greatest avidity for iodine and the greatest ability to produce thyroxine and diiodotyrosine.

An extensive study involving 94 cases of nodular goiter, 16 of these with carcinoma, was subsequently undertaken by Dobyns and Lennon.[36] They found a parallelism between the degree of function and cellular differentiation of the adenoma, with certain exceptions. There were adenomas with cellular hypertrophy and hyperplasia which were hyperfunctioning, as well as adenomas both with hypertrophy and hyperplasia which barely functioned at all. This latter group with negligible function showed an increased variability in cell height. In this respect they were thought to shade off into the class of tumors known as papillary adenocarcinomata.

At first it was reported that malignant thyroid tumors have no avidity for radioiodine, while the surrounding normal tissue colloid did.[34] However, the work of Dobyns and Lennon,[36] as well as that of other investigators[37-38] soon demonstrated that there are exceptions, depending upon the type of tumor, whether primary or metastatic. The uptake of iodine was found closely linked with the structural qualities of the tumor—the cellular arrangement in the follicular pattern and the presence of colloid-like material. Moreover, the degree of function of these tumors roughly parallels the histologic differentiation. This is recognized in radiotherapy.

Radioautograms were made of the thyroid glands of 47 selected patients with carcinoma of the thyroid given tracer or therapeutic doses of radioiodine (I_{131}) prior to surgery. Twenty showed retention of the isotope in some portion of the neoplastic areas.[38] Papillary adenocarcinoma of the thyroid retained no radioactive iodine; other papillary adenocarcinomas with follicular or alveolar patterns showed retention in five of eight cases, while two-thirds of the carcinomas showing follicular and alveolar types throughout, stored radioiodine. Differences in the amount of radioiodine collected were also observed in other types of malignant thyroid tumors. In only two histologic components of thyroid carcinoma was radioiodine found—in the alveoli and even more in the follicles with colloid.

Beginning with the work of Hamilton and Lawrence[39] who reported almost complete destruction of the thyroids of dogs and rabbits with radioiodine (I_{131}), without evidence of damage to other body tissues, radioiodine has been used therapeutically for patients, with increasing frequency, in the treatment of hyperthyroidism and now more in the treatment of more "hopeless" patients with malignancy of the thyroid.

Radioiodine given in adequate doses will subtotally inactivate the hyperfunctioning thyroids in patients with Graves' disease and thereby produce what has been considered a satisfactory remission of the symptoms and signs of hyperthyroidism.[40] Thus far, during the brief span of years over which this form of therapy has been applied, the chief complication has been myxedema and this is reported in but a small percentage of cases.[40-41-42-43]

A three to five year report on the early experiments with radioiodine therapy of 29 patients with hyperthyroidism showed a high effectiveness in 80 percent[41] of the cases. Similar results were obtained by Chapman and Evans.[42] Chapman[43] reported that of 65 patients treated with the 12-hour isotope, 51 responded and continued well, 11 were overtreated and developed hypothyroidism and three improved but remained toxic. With the eight-day isotope (I_{131}) available more recently, results showed the average interval for attaining a normal basal metabolism to be about two months. No relapses or recurrences were noted. A few developed myxedema and none in this particular series had radiation sickness. Radioiodine (I_{131}) was thus considered an effective therapeutic agent. The possibility of a late carcinogenic effect, however, can only be settled after a long period of subsequent observation.

In recurrent toxic goiter which did not respond to other treatment, an 89 percent remission rate was noted subsequent to the administration of radioiodine. This was considered an indication of the value of this form of therapy in the treatment of this type of hyperthyroidism.[30] Its value in primary hyperthyroidism as compared with surgery combined with other forms of treatment, was not so striking.

In view of the reported successes of radioiodine therapy in Graves' disease, this type of treatment was instituted in the management of thyroid tumors. Meanwhile, the groundwork was being laid with autographic and chemical studies showing the extent to which these tissues could be expected to collect radioiodine.[35-36-37-38]

The limitation of the ability of these tumors to collect iodine, which would diminish the success of radioiodine therapy, made it necessary to find some means of increasing this particular function of these tumors as well as of their metastases.

Attempts to increase the efficacy of radioiodine therapy were next undertaken. They are of particular interest because they may give a clue, in particular, to the handling of the otherwise unmanageable metastases of even other tumors throughout the body. Seidlin and his associates[44] found that the uptake by metastatic thyroid carcinoma is more closely correlated with the degree of preceding thyroidectomy than with the histologic structure of the metastasis. In those patients in whom initial studies with radioiodine do not show concentration in the metastases, such concentration could be induced by either thyroidectomy (surgical, radiation or chemical) or by injections of thyrotropic hormone.

Seidlin further found that[45] metastases are unlikely to show any radioiodine uptake unless the primary tumor has destroyed most of the original non-neoplastic thyroid gland. Thus, if no radioiodine is taken up by the metastases, a complete thyroidectomy in his opinion is indicated. About five or six weeks after thyroidectomy, or earlier, the metastases begin to show an uptake of radioiodine. Large doses should then be continued at fairly frequent intervals.

In 27 patients, studied by Rawson and his group,[37] total thyroidectomy or the administration of large doses of radioiodine led to significant increases in the iodine-collecting capacity of the metastases. This was noted in follicular or solid adenomatous types, however, and not in papillary adenocarcinomas. The use of thyroid stimulating hormone along with the thyroidectomy would further increase the avidity of the metastases to take up radioiodine. The administration of thiouracil resulted in myxedema but did not produce a block to the utilization of iodine, comparable to that usually observed in patients with Graves' disease when receiving this drug. These observations, it was thought, might indicate that the mechanism by which functioning thyroid carcinomata concentrate iodine, is of a different nature than that of normal thyroid tissue.

While there have been striking tumor regressions and over-all improvement in physical well-being, evidence is still lacking that such a remission will be permanent. Also, fairly serious complications of this form of therapy have been reported.[46]

The use of radioiodine in the investigation and management of thyroid disease has been of stimulating interest. The findings, however, are in the developmental phase and should be carefully evaluated before any final conclusion may be drawn. Experience is not yet sufficient to warrant any widespread general use in therapy.

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AMONG THE SPEAKERS AT THE SURGICAL DAYS IN VIENNA
(Austrian Chapter, International College of Surgeons)
ON JULY 1 AND 2, 1949
ARE THE FOLLOWING

FINSTERER, MANDL, PAOLUCCI, DEMEL, SCHÖNBAUER, DOGLIOTTI, PLENK, ERLACHER, SCHLANDER, CHIARI, LORENZ, HARTWICH, ANTOINE, ZACHERL, NAVRATIL, HEIDLER, WERNER, RICHTER, ZDANSKI, ZAUNBAUER, STEINDL, STARLINGER, HRYNTSCHAK, THOREK (MAX), HUBER, REISE, KNOFLACK, McNEALY, THOREK (PHILIP), HALL, ANDREASEN, SOLERROIG, CUNHA, ATKINSON, ALEXANDER, JEWETT, FOURNIER and OTHERS.

Thyroidectomy—The Prevention and Treatment of Complications

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THYROID disease is unequalled in possibilities of complications following surgery, for as Hertzler[1] says: "Through the nature of the disease, we have nervous, circulatory, nutritional manifestations, with limitless possibilities." Thus, for a surgeon to accept full responsibility of the thyrotoxic case would be unfair to the patient, to society and to himself. The burden of diagnosis is shared in the cooperation with the radiologist, the laryngologist, and the internist. The anesthetist participates in the successful outcome of surgery, even with operations accomplished under local anesthetic.

The decision for operation should be based upon a comprehensive physical examination and a complete investigation of the patient's mode of life, occupation, medical history, mental status, and current symptoms. The question of *when* to operate must be determined by examination findings and the patient's response to any preparatory procedures which may be indicated. Surgery never should be undertaken less than several weeks after an acute respiratory infection has subsided and oral hygiene, so often neglected preoperatively, must be routine, as with any surgery that requires bed rest. I am convinced that more postoperative throat and chest complications result from diseased or infected teeth than previously have been acknowledged. The complete confidence of the patient in the attending doctors is an important consideration in the prevention of the anxiety and hysteric states often encountered postoperatively in maladjusted patients.

The thyrotoxic patient must be evaluated by the internist, especially the cardiac aspects of the case which to some degree are coincident with all toxic thyroid disturbance. The individuals with heart damage require more than passing comment for where there is, or has been, heart involvement, the regimen of a cardiac patient is necessary. Administration of propylthiouracil to the thyrotoxic patient should be initiated and continued, accompanied by frequent determinations of the basal metabolic rate and laboratory examinations of blood, until the B.M.R. is lowered or stabilized. Following discontinuance of the drug, Lugol's solution is then advocated for a time prior to operation.

The surgeon must be familiar with the gross pathology and anatomy of the thyroid gland and of its associated structures. Physical examination or routine fluoroscopic and roentgenographic investigation may indicate the presence of a substernal goiter and determine the position of the trachea. Both pre and postoperative visualization of the vocal cords in patients, who have had voice changes or previously have been operated, is essential. Laryngeal examination preoperatively shows in many cases some lack of mobility of one or both vocal cords.

Pemberton[2] states that the first group of hazards includes not only accidents of technic, which are for the most part avoidable, but also errors of surgical judgment, particularly in deciding when to operate and in selecting the surgical procedure. The second group of hazards are presented by cases in which other diseases are associated with exophthalmic goiter. He believes that liver failure occurs consequent to thyroid disease and that hepatic changes, which perhaps are most serious, may be prevented by early surgical treatment. However, a careful, unhurried, approach to operation is absolutely essential. Hagen[3] emphasizes that the surgeon operates to cure and recurrences are best prevented by a careful appraisal of the patient.

Liberal thyroidectomy and careful follow up will eliminate the factors responsible for the initiation of the disease. The physiologic restoration of the thyrotoxic patient requires

something more than the mere routine of rest, Lugol's solution, sedation, and vitamins "BW and C." These are important, perhaps vital, but they are with the exception of the vitamins merely transient accessories to the final conquest of the malevolent disease. Complete thyroidectomy, according to the teachings of Hertzler, is being more generally accepted, especially by the younger surgeons and apparently is not necessarily followed by the myxedematous stage which has been the subject of controversy. Partial thyroidectomy is a technic not of choice, but of necessity. Prudence may obligate a surgeon to choose partial thyroidectomy before or during an operation, but we know from experience that if we operate in the true incipient stage we will have almost one hundred percent permanent cures and practically no deaths.[4] DeCourcy[5] states it is better to remove too much, rather than too little of the thyroid gland.

Despite the best medicosurgical judgment and experience every surgeon occasionally meets misfortune owing to conditions which cannot be foreseen. Death following thyroidectomy, in the light of our present day knowledge, should be rare. However, since we are dealing with the human body and other complex factors, deaths will continue to occur, even with the most careful preoperative examination, preparation, and ideal operative procedure and careful postoperative care. These are as unpredictable as life itself. It behooves us to realize this and adjust ourselves to the acceptance of all possible assistance—whether it be laboratory and clinical service or social and professional advice.

Among the contraindications to immediate thyroidectomy are: uncertain diagnosis; previous indiscriminate use of iodine, especially in nontoxic adenomatous glands; failure to respond to preoperative therapy; persistent nausea and vomiting; infection which might be eliminated; unfavorable cardiac conditions; and, deterrant behavior of the patient. Dixon[6] believes that mortality is usually attributable to errors in preoperative preparation, in selection of time for surgery, and to postoperative complications. As possible causes, or contributing factors, I believe we should add to these: incorrect diagnosis; hemorrhage; tracheal collapse; thyroid crisis; toxemia; complicating liver damage; embolism; complicating carcinomatosis; and inexperienced surgical judgment and comprehension of existing pathology.

OPERATIVE AND POSTOPERATIVE COMPLICATIONS OF THYROIDECTOMY

Many surgeons prefer a planned incision with good exposure, ample division of the muscles for proper visualization of the gland and structures, rather than a smaller incision with greater trauma from the increased retraction required. Clear observation and unhampered dissection anatomically is better surgery than blind removal or blunt separation by finger elevation and retraction of the gland. Boehem[7] describes special anatomical dissection with control of bleeding, especially in hypertension cases. If bleeding cannot be brought under control, it is better surgical judgment to pack a wound and discontinue an operation, than to chance additional trauma.

Aspiration of large cystic adenomata prior to removal, especially those of the substernal type, frequently prevents damage to adjacent vessels from tugging and tearing. Lahey[8] suggests the employment of a semiflexible tube in intrathoracic goiter prior to operation.

Hemorrhage, especially from the superior thyroid artery, is always a danger. To prevent the ligature on the superior thyroid artery slipping, transfixion of the pole is suggested. Meticulous ligation of all bleeding points with isolation of the veins and arteries from adjacent tissues and utilization of fine ligatures are necessary to minimize subsequent serum formation. Encouraging straining, coughing, and gagging by the patient before closure of the wound should be routine to assure the surgeon of complete hemastasis. Drainage may be used if considered advisable but, if employed, early removal is advocated to reduce scar formation. If a hematoma develops it must be evacuated even if reopening of the incision is necessary. Wound infection is rare and must be attributed to uncontrolled technic, or self-infection. When encountered treatment is by inside open drainage and chemotherapy and secondary closure.

The prevention of the many complications which arise in the postoperative recovery of the thyroidectomized patient has not been stressed sufficiently in the literature. Clute[9]

feels that if there is any single complication following thyroidectomy, which is more trying than any other in the first few days or weeks of convalescence, it is the development of serum underneath the skin flap and that serum follows incomplete hemostasis or the inclusion of too large pieces of parathyroid muscles or large pedicles and the use of coarse ligatures.

Almost any extensive operation within the neck is followed by some disturbance of speech owing to congestion of mucous in the larynx or trachea, to manipulation, or to interference with one or both recurrent laryngeal nerves. Lahey[8] for years has advocated visualization of the recurrent laryngeal nerve and his policy of routine demonstration of this important structure, although not accepted by all thyroid surgeons, has proved itself to the satisfaction of a great number.

The postoperative neck and scapular pains which are usual complaints of older patients are attributable to faulty position of the patient during operation. The difficulty in breathing and swallowing frequently encountered, usually results from trauma of the trachea or edema of the larynx and esophagus. It may be relieved by bending the head forward, encouraging the liberal use of fluids and stimulating cough reflexes.

Seabrook[10] considers embolism an important complication in thyroid surgery and in 1929 published six cases. Larson[11] reports that embolism may result from introduction of air into the blood stream through veins which have been cut necessarily during operation, or from trauma or accidental tearing of veins which has occurred without becoming apparent. He advocated ligature before division of any vessel of size. If the condition has developed, administration of caffeine and artificial respiration are indicated.

Sommer[12] believes that a considerable percentage of the patients who die from hyperthyroidism, do so because of embolism. These deaths occur usually in the face of a long standing disease.

Tetany may develop seven to 12 hours following thyroidectomy from injury or removal of one or more parathyroid glands, or interference with the circulation of blood to them. The parathyroids usually are situated outside of the thyroid gland, but frequently at times are found closely associated with, or imbedded in, the gland itself. The surgeon must recognize these important bodies to avoid interference with their function by injury during operation.

Symptoms of tetany also may be attributable to hemorrhage, to pressure from formation of a hematoma, or to edema from trauma to the adjacent tissue. Pemberton[13] states that ligation of the inferior artery proximal to entrance into the thyroid gland causes no interference with the parathyroids. However, blood calcium estimation and laryngeal observation preoperatively are mandatory, especially in cases of reoperation. Trousseau's Sign (carpopedal spasm) produced by pressure on the arm is an indication of beginning tetany. Tetany usually is evidenced initially by restlessness, twitching, cramps and spasms of hands and feet.

Tetany may be transitory and respond to administration daily of 10 cc. of five percent solution of calcium chloride, intravenously accompanied by vitamin B therapy. With mild cases 10 grains of calcium chloride per day, orally, or cod-liver oil may be used with success. Some surgeons routinely give patients postoperatively five cc. of five percent calcium chloride per day intravenously, or cod-liver oil by mouth for a period of time. No sound reason to condemn this procedure is apparent. Severe tetany may require administration of parathyroid extract accompanied by calcium gluconate intravenously, in amounts and over the period of time necessary to eliminate symptoms of the deficiency.

The postoperative crisis or storm which occasionally follows thyroidectomy usually develops about 36 hours after operation with rapid pulse, fever, and sometimes delirium. Inadequate preparation of the patient is commonly given as the cause. When encountered, crisis may be treated satisfactorily by intravenous chloride and sodium bicarbonate, vitamin "B three times daily, 0.5 gm. of liver extract per day (2), sedation of choice, and cooling ice bags.

Injuries to the recurrent laryngeal nerve has been emphasized by Lahey,[8] Mulligan,[14] Green,[15] Scheicher,[16] and Bachhuber.[17] Different exposures, methods of enuclation, and

advantages of freeing the lower pole first, or the reverse, have been debated for years, which has proved to the author that a specific standard cannot be established. The recurrent laryngeal nerve may occupy different positions, especially in relation to the inferior thyroid artery, but if the inferior artery is ligated well lateral to the capsule, the possibility of grasping the nerve is lessened. In complete thyroidectomy it is conceded that visualization of the nerves is essential. However, if a subtotal thyroidectomy, as in many adenomatous glands, suffices, I see no reason to seek trouble by invading a mined field.

When interference with the recurrent laryngeal nerve is suspected or damage actually has occurred, Lahey[8] advocates repair with china silk, on blood vessel needles. He also states that those cases recognized in the postoperative convalescence, must be repaired in the following three-month period. Edema of the oversewn capsule may be responsible for some voice change or temporary cord paralysis.

Laszo[18] calls attention to difficulty in swallowing which may result from injury to the laryngeal nerve, which may be caught with the suture when ligating the superior thyroid artery. If the condition of dysphasia persists after six months it is probably nervous in origin and may be verified by fluoroscope examination with a barium meal and explained to the patient.

Severe disturbance six to eight months following thyroidectomy is probably the result of scar formation and requires surgery to free the cord. A paralysis of one cord is usually compensated in time. Paralysis of both cords, due to secondary edema, produces voice change which is probably temporary and will correct itself. But, if improvement does not occur—tracheotomy is indicated, and perhaps the King operation will have to be considered. For permanent bilateral abductor paralysis Lahey suggests a tracheotomy tube fitted with a Tucker valve, which permits the patient to retain an excellent voice without closing the tube by digital methods. If the tube is not well tolerated, submucous resection of the cord is indicated.

Laryngitis or tracheitis may be instigated by aspiration, infection, or trauma from operative manipulation or interference. The condition should be countered by measures of stimulation or interference with nerve control: 1. Inhalation from steam tent, with Balsam of Peru added; 2. syrup of hydriodic acid, brams 1, p.r.n.; 3. lemon drinks; 4. force fluids; 5. chewing gum, to promote salivation; 6. chemotherapy of choice.

Tinker,[19] in 1940 advocated tracheotomy prior to operation in carcinoma of the thyroid.

In postoperative trachea distress, a temporary tracheotomy may be required for only a few days, and is better surgical judgment than a sleepless night from regret. Tracheotomy is usually done about the second ring and may require a tube larger than the one ordinarily used in a tracheotomy. The procedure may be indicated by collapse of the trachea following relief of the pressure on its thinned-out wall; by persistent cyanosis, even after the relief of hemorrhage, and by abductor paralysis from interference with the recurrent nerve.

Intrathoracic goiter can be differentiated from a fibroma arising in the esophageal wall by fluoroscopic observation of a barium meal.[20] Carotid sinus syndrome is corrected by 10 cc. of one percent procaine solution injected at bifurcation of carotids and 0.01 grain of atropine sulphate intravenously.[21] In diabetes, thyrotoxicosis may be coexistent and each may aggravate the other. Control of the diabetes is absolutely essential. In some cases thyroidectomy has aided the diabetic therapy: in others, control of the diabetic condition has reduced the toxicity of the thyroid.

Massive collapse or Atelectasis is not a common postoperative complication, but is frequently overlooked temporarily. It is usually portrayed by elevation of temperature (103°-105°), increased pulse rate, dyspnea, and apprehension of the patient produced by inspissated mucous.[22] This complication can be averted by good nursing care, which includes changing the position of the patient frequently, encouraging coughing, and assuring liberal fluid intake. Atelectasis may be verified by x-ray examination of the chest and a sharp, severe slap on the back may encourage the dislodgment of the mucous plug, according to Rustin[22] from his experience with the anesthetic service of the Royal Canadian Army Medical Corps. Failure of this procedure ne-

cessitates bronchoscopic examination and removal of the obstruction in the bronchial tree by aspiration.

Pneumonia still occurs occasionally following thyroidectomy, but today is less frequent. Careful preoperative examination, preparation, treatment, and dental hygiene have been followed and surgery is supplemented with the postoperative use of oxygen and chemotherapy. Pneumonia should be rare.

Pulmonary abscesses result from unrecognized, initial bronchial obstruction with resulting infection and abscess formation and are treated by bronchoscopy aspiration, irrigation, and chemotherapy.

Toxemia may follow thyroidectomy, frequently as a result of incomplete examination and neglect of existing preoperative condition. The inciting factor also may be the contraction of an illness at the time of operation or immediately thereafter. Most of us are too prone to classify all toxemias in the latter category. Fortunately, with the newer chemotherapeutic drugs and antibiotic agents these conditions respond favorably.

Exophthalmous usually disappears after the patient has been thyroidectomized, but in some instances it persists even with improvement of all other symptoms. Other cases after operation show progressive exophthalmous though the condition had not existed previously. Ceballos[23] speaks of this as malignant exophthalmous and quotes Lahey as stating that loss of sight menaces in all cases of pre and postoperative exophthalmous. On the other hand, Hertzler has never seen a case of malignant exophthalmous. The Naffzeger operation probably offers the best hope for recovery but should not be delayed until ulceration of the cornea is established.

An excellent scar following thyroidectomy is determined by a carefully planned incision with meticulous control of all bleeding points and precise closure employing fine ligature material with close approximation of the skin edges, preferably with clips, and early removal of drains if used. Serum should be recognized early and evacuated immediately. Alcohol dressings on the neck for the first three days postoperatively and early massage if edema is present, enhance clean, loose scar formation. However, if dimpling of the scar results and is not responding to massage, early undercutting followed by massage is usually advantageous. Keloids respond fairly satisfactorily to low doses of x-ray.

When confronting a patient at "followup" examination a surgeon may be embarrassed by having overlooked, the pyramidal lobe at operation months earlier, especially if the individual presents symptoms of recurring hyperthyroidism. Pemberton[13] says that myxedema may follow thyroidectomy and upon treatment with thyroid extract symptoms of hyperthyroidism may reappear. This situation may be averted by care in administering thyroid extract postoperatively. One-half grain three times each day for a period of 20 days followed by a recheck of symptoms is recommended as preferable to the usual one grain per day for an indefinite period.

The term recurrent thyrotoxicosis has been loosely used and there are many exponents of the thesis that a so-called recurrent thyroid is only an incomplete thyroidectomy. Bothe[24] stated that hyperthyroidism recurs after thyroidectomy in two of three patients. Thompson[25] makes a distinction between recurrence and persistence of thyrotoxicosis. Recurrences are best prevented by a careful appraisal of the patient, by a liberal thyroidectomy, and by a carefully planned follow-up that will eliminate the factors responsible for the initiation of the disease.[3]

A few years have brought a tremendous increase in our knowledge of thyroid disease and its concomitant effects upon body processes, and in the methods of treating the disease and its sequelae. Concerted efforts of surgeons, physicians, especially internists, physicists, and chemists have resulted in a vast reduction of mortality and morbidity from disturbances of thyroid function. With continued research for better methods of diagnosis, better technics of surgery, better control of patients during operation with adjuvant procedures, and improved facilities for averting and treating postoperative complications —we may soon have the means for prevention as well as cure of the hyperthyroid individual.

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Partial and Total Intrathoracic Goiter

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THE diagnosis of intrathoracic goiter is often delayed and its presence is usually not determined until some one particularly interested in thyroid disease suspects an intrathoracic projection and takes a roentgenogram of the chest. Sometimes a nodular mass is felt above the clavicle and a suspicion is aroused that there is a tumor or mass in the upper mediastinum. Mechanical symptoms of cough, shortness of breath, difficulty in swallowing and hoarseness are too often not attributed to intrathoracic pressure.

Goiter was first noticed to extend deep into the thoracic cavity in 1749 by Haller, an anatomist. Dubourg in 1826 reported the first clinical observation of intrathoracic goiterous projections. Malignancy of an intrathoracic goiter was noticed by Adelmann in 1828. Malord in 1879 reviewed the French literature and found 11 cases. With the discovery of the x-ray in 1895, the diagnosis became more apparent. Wuhrmann in 1899 analyzed the reports of 91 cases of which there were 16 malignancies.

The condition is more common in women, and should be naturally so, as nodular goiter presents itself more frequently in the female sex. Jackson found 23 total intrathoracic goiters in women out of a series of 25 cases.

In goiterous belts the partial form of intrathoracic goiter may range as high as 25 or 30 percent, while in non goiterous sections it is reduced to 10 percent or less.

Crile reports an instance of less than one percent. I have found 48 partial intrathoracic goiters and seven total masses in 650 cases.

What really constitutes an intrathoracic goiter rests largely with the conception of the amount of gland necessary to protrude into the chest before such a term is appropriate. To some it may appear that a goiter is intrathoracic when a relatively small portion extends into the thorax; to others it may seem necessary that the vast majority of the goiterous mass should be in the thorax before such a term is applicable. I believe the mass should extend down to or near the aorta. Certainly a large portion should be found extending well through the thoracic aperture in order for the term intrathoracic goiter to be accurate. In fact, a truly intrathoracic goiter is one in which the entire mass is within the thorax.

DEFINITION AND CLASSIFICATION

Curtis has clearly divided projections through the thoracic aperture into the chest by defining the aperture itself. He describes the plane of the thoracic aperture as an imaginary plane extending from the top of the first dorsal vertebra to the superior part of the manubrium and spreading out laterally over the first ribs. Goiters protruding below this plane are classified as deep cervical, partially intrathoracic, and totally intrathoracic. The deep cervical lesions are those masses whose lower portions protrude below this plane, but on swallowing the lowest projection can be elevated above this imaginary plane and palpated in the neck.

The partially placed intrathoracic goiter extends deep into the chest and does not arise into the neck on swallowing, nor can it be elevated above the thoracic aperture at will. These protruding masses sometimes become fixed against the first rib by a deep groove and do not move freely up and down on swallowing or with respiration. This fixation often causes serious respiratory difficulty by deviation and narrowing of the trachea.

The complete or totally intrathoracic goiters are entirely placed within the thorax and no portion arises up into the neck under any circumstances. It doesn't matter whether this goiterous mass is found wholly behind the sternum, in the mediastinum, or deep within the chest. It is intrathoracic, and the term is still applicable although the classification of sub-sternal, mediastinal, lateral, pre-vasal, and post vasal, or post visceral are likewise appropriate and more descriptive.

It is interesting to note that the only emer-

gency that occurs in thyroid surgery is that when a pedunculated cervical mass descends into the chest and becomes impinged beneath the first rib and produces an acute angulation or compression of the trachea with resulting respiratory obstruction.

METHOD OF DEVELOPMENT

The intrathoracic position is assumed from one of three causes. It may be an independent growth of an aberrant portion of the original thyroid which has become detached from the parent gland in its descent during fetal life or thyroid tissue may have been carried along with the thymic stalk. Or, what is more probable, it is the direct extension of a discrete nodule in either of the lower poles or the isthmus of the thyroid gland. It is true that small remnants of the thyroid may be detached during fetal descent and live independently of the parent gland and, subsequently, develop thyroid pathology in unusual locations. Such descent to the depth of the thorax is rare. This may be said, likewise, of remnants that descend with the thymus.

An intrathoracic goiter results, therefore, from the downward growth of an isolated nodule in one of the lower poles or the isthmus of the thyroid gland which follows the line of least resistance into the chest, being carried along and aided in its descent by the up and down movement of swallowing, by the fascial planes, and by the bony and muscular restrictions to outward extension. The chest, sternum, and vertebral column tend to converge at the thoracic aperture, and make it most difficult for nodular goiterous masses to ascend into the neck when once the thoracic cavity has been invaded. Enlargement and growth in any other than the downward course is, therefore, prevented. If the original nodule springs from the isthmus or left inferior pole of the thyroid, it is directed toward the left by the mediastinal vascular structures. Lesions from the right are, likewise, often directed toward the left by the large innominate vessels.

With the descent of the nodular growth, there is carried along the cervical and mediastinal fascia which form the capsule around the mass. The goiter is usually attached by a more or less definite pedicle to the cervical gland, but this pedicle may be very thin or even obliterated as a result of the long standing effect of swallowing, movements of the neck, and respiration. Complete absence of all former connection or of evidence of a thin pedicle is extremely rare. The blood supply is carried downward from above. The superior and inferior thyroid arteries descend with the gland as it invades the chest. The blood supply is from above downward, a point to remember at operation.

TYPE OF GOITER

The goiterous mass is usually nodular and is subject to the same pathological changes seen in cervical nodular goiter. Cyst formation, calcification, hemorrhagic degenerated areas and malignant changes occur as elsewhere. The colloid is thin and pale, and the spaces are often filled with evidences of recent or old hemorrhage. The arteries and arterioles are damaged and frequent hemorrhages occur. An extensive hemorrhage may produce sudden respiratory difficulty due to marked increases in the size of the mass. The central portion of a large goiter may liquefy due to an insufficient blood supply, and form degenerated cysts. Variable size cysts often result from hemorrhage into the tumor mass. Epithelial activity is rarely present due to poor vascularity and degenerative changes.

One of the tragedies of intrathoracic goiter is the development of malignancy. It may not be positively diagnosed except by microscopic section, but is suspected by vocal cord paralysis due to recurrent nerve involvement, restriction of the tumor mass in the up and down movement of swallowing and coughing, irregular progressive enlargement of the lesion, lung metastasis, and collection of fluid in the pleural cavity.

Constriction of the trachea may occur, necessitating the division and separation of the pretracheal muscles to afford room for outward extension of the cervical portion of the growth. Bony decompression may be necessary. Tracheotomy is difficult to perform because of the inaccessibility of the trachea below the tumor mass. Lesions totally intrathoracic expand in all directions, pushing structures aside as they enlarge.

SYMPTOMS

The symptoms are rarely the toxic manifes-

tations as seen often in cervical nodular goiter, are largely mechanical and depend upon the structures pressed. These are respiratory or vascular. The trachea is usually pushed to one side and markedly narrowed from pressure, resulting in dyspnea, cough, emphysema, and sometimes, when a bronchus or trachea may be markedly flattened by pressure from behind or in front. Change in body posture may angulate and increase tracheal pressure causing respiratory effort. A narrowed deviated trachea reduces oxygen intake resulting in increased heart effort and increased respiration, thus adding to the strain of an already damaged thyroid heart.

Pressure sensations, a tightness in the chest, and difficulty in swallowing may not be pronounced, as very large growths seem to accommodate themselves with a minimum of discomfort. Pressure upon the large vessels, especially the internal jugular veins may produce marked enlargement of the veins of the chest and neck with a great amount of swelling of soft tissues from back pressure and increased venous tension. Sudden release of this pressure may result in severe and sudden alteration of the venous pressure of the brain. Lahey has suggested that it is wise in severe cases to divide the pretracheal muscles and at times disarticulate the manubral-clavicular joint to afford gradual release of intracranial pressure sometimes before removing the mass.

The diagnosis is made by the analysis of the symptoms by an obvious cervical goiter with intrathoracic projections, by the presence of any of the above physical signs, and by the roentgen ray. Any suspicions should be followed by a roentgenogram. It is important to make lateral as well as anterior posterior roentgenograms to determine the relation of the trachea to the goiterous mass, and position and degree of tracheal compression.

SURGICAL APPROACH

The operative approach for an intrathoracic goiter is a low collar incision. It is rarely necessary to enlarge the thoracic opening by any of the surgical methods upon the bony structure.

It is extremely valuable to introduce a catheter into the trachea if the goiter is large and there is constriction and deviation of the trachea. A large goiter extracted through a tight fitting outlet may so obstruct the trachea that serious respiratory difficulty may develop during the process of delivery.

With an intratracheal catheter in place, a large intrathoracic goiter may be delivered through the thoracic aperture with the minimal embarrassment to respiration. The use of helium with oxygen will permit a larger amount of oxygen to be delivered through a narrow constricted trachea and materially reduce anoxemia.

It must be remembered the blood supply originates from above, and passes downward into the chest with the descent of the goiterous mass. Hemorrhage is controlled by first ligating the superior thyroid artery, after which a resection of the cervical thyroid from the trachea, and division of the isthmus will facilitate the subsequent removal of the intrathoracic mass by accomplishing mobility of the tumorous attachment and establishing more freedom of manipulation. The inferior thyroid and lateral vein are, likewise, ligated as they become accessible. Vascularity within the chest is limited as the mass is surrounded by the cervical and thoracic fascia which has been pushed down with the descent of the goiter.

Approach to an intrathoracic growth is best accomplished by passing the index finger from behind along side of the mass and freeing it posteriorly, laterally, working to the lowest point of the mass and lifting it out of the thorax rather than partially freeing it and attempting to draw it out by traction. A considerable negative pressure is present, and prevents the delivery of the goiter until air is permitted to pass between the capsule and the goiter. This often markedly elevates the goiter and makes it more accessible. Forceful traction may pull on adherent bands attached to the side of the goiter and increase its anterior posterior or lateral dimensions, making delivery harder or impossible. Again, traction on adhesions may seriously damage some adherent blood vessels, or produce an angulation or tear into a softened trachea. The posterior lateral approach affords more freedom of action by entrance through the soft areolar

tissue near the tracheal groove than one between the sternum and the growth.

Hemorrhage is not great, and is controlled by packing. Small spurters should be carefully picked and ligated. The cavity, though large, may almost immediately be eliminated by shifting of mediasterial structures and lung expansion. Adequate drainage should be established and maintained to prevent accumulation of serum, infection and a fatal mediastinitis. Large unobliterated cavities should be packed or well drained to prevent bleeding, oozing, and accumulation of body fluids. The recurrent nerve is usually pushed by the large goiter mass well into the groove between the trachea and the esophagus, and is rarely injured if the capsule is carefully dissected and the tumor mass gently manipulated. The recurrent nerve should be exposed.

If piece meal removal has been employed, no remnant should remain to necrose, prolong the drainage, and add to the danger of infection and mediastinitis. The removal of large cysts may be facilitated by evacuation of the contents.

Gentleness is essential throughout the operation. It lessens the possibility of hemorrhage from adhesions to deep vascular structures and reduces the possibility of tracheal compression, collapse, or perforation. After removal of the tumor, the trachea eventually returns to its normal position.

SUMMARY

The following headings have been considered in this article:

1. What constitutes an intrathoracic goiter.
2. Curtis description of classification.
3. Manner of development of intrathoracic projections and anatomical consideration of importance bearing upon surgical removal.
4. Nature of pathological changes.
5. Technical steps in the surgical removal.
6. Indications for simple drainage or packing.

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Important Anatomical Structures in Thyroidectomy

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MANY surgeons still regard a goiter as a "sort of a tumor." As a result in a thyroidectomy, they proceed in cutting and tying the vessels as they bleed without any attention to the anatomy involved, the most important of which is the blood supply. This may succeed in the hands of a skilled surgeon, but controlling the hemorrhage is very difficult and the method is not advisable in the hands of the average surgeon who performs an occasional thyroidectomy.

At the present time, the problem of mortality is of little concern no matter what method is used in a thyroidectomy. It will be the purpose of this discussion to show that the thyroid surgeon can obtain the best mortality, cosmetic, and functional results, as well as the avoidance of technical complications such as injuries to the laryngeal nerves, parathyroid bodies, and the occurrence of hemorrhage, if he follows a careful technic based on the anatomy involved in the excision of a goiter.

The surgeon must remember that the thyroid may present certain anomalies in shape and position which are of surgical importance. The pyramidal lobe, so often the source of recurrence if not removed, at times may be absent. It may be double in others. The isthmus may be missing as in the thyroid of a dog. According to Stierlin, absence of one of the lateral lobes occurs once in a thousand times. We recently had such a case. Thyroptosis, retrotracheal and retroesophageal position may exist. Accessory glands are at times present along the course of the thyroglossal duct from the foramen caecum. Lingual goiters while rare, do occur. A recent case of ours had a large goiter at the base of the tongue just over the epiglotis. Excision caused marked hypothyroidism. Accessory glands can occur within the trachea and within the thorax.

The surgeon must also be conscious of the fact that while the parathyroids are usually situated external to the thyroid on its posterior surface between it and the thyroid fascia, they may be found anywhere on the capsule. Occasionally, they have been found on one of the main thyroid vessels. They usually occupy one of three positions—high, medium, or low.

As the operation is begun, the surgeon must have in mind the cosmetic result. Therefore, he must place his incision in such a way that the scar will fall at a point at the junction of the neck with the sternum. This may seem trivial to the surgeon, but it is of considerable importance to the patient. Scars that postoperatively are below this level usually become wide and ugly. It must be remembered that the larger the goiter is, the higher the incision should be made. When the healing wound is slightly above the sternoclavicular joints, the skin and subcutaneous tissues are more flexible and a neater result is obtained.

As the incision is deepened, the operator must also be mindful of the possibility of air embolism. While this is a rare complication, it does occur and must be taken into consideration, particularly in dealing with a patient with severe hyperthyroidism. The veins in the anterior and posterior triangles pierce the cervical fascia obliquely. As a result, they remain open when incompletely severed. This accounts for the occasional case of air embolism in thyroidectomy and in the excision of carcinomatous glands in the posterior cervical triangle.

The usual location of the thyroid incision is at the level where the anterior jugular veins pierce the superficial layer of the deep cervical fascia. At this point the veins penetrate the fascia at an oblique angle (Fig. 1). If the incision only partially bisects the veins, the veins are held open and air is sucked into the lower end. This can occur more often in a patient with hyperthyroidism because with the extremely fast pulse much air rapidly enters the heart. The contractions of this organ on a frothy blood is occasionally accompanied by sudden death.

The anatomical relationship of the thyroid

Fig. 1. Dissection showing the oblique passage of the anterior jugular vein thru the deep cervical fascia.

to adjacent structures is of primary surgical importance. The most important organ in relation to the thyroid gland is the *larynx*. Immediate death from hemorrhage occurs very seldom in the modern thyroidectomy, but injury to the recurrent laryngeal nerves still occurs too often. It is one of the most disastrous complications for the patient, and a most discrediting factor to the surgeon's reputation. Injury to the laryngeal nerves can be avoided by following a technic based on an anatomical approach.

The larynx which is so intimately related to the thyroid gland, lies ventral to the fourth and fifth cervical vertebra. The normal thyroid, from 20 to 30 grams in weight, is sit-

ated over the front and sides of the upper (second to fourth) tracheal cartilages and the lateral lobes extend upward on either side of the larynx. Pathological changes in the thyroid often displace and distort the trachea and the larynx, and the surgical treatment of these disorders occasionally injures the nerves of the larynx, thereby interfering with its functions.

The musculature and innervation of the larynx are worthy of a brief review. The muscles of the larynx are divided into the extrinsic and the intrinsic groups. The extrinsic group which comes from neighboring parts to be inserted on the larynx and acting on the voice box as a whole are innervated by the external branch of the superior laryngeal nerve. The intrinsic muscles confine themselves strictly to the larynx and control the functions of phonation and respiration, in which we are interested. The intrinsic muscles of the larynx are (1) the posterior crico-arytenoids, (2) the lateral crico-arytenoids, (3) the thyro-arytenoids, (4) the interarytenoid and (5) the cricothyroids. These muscles are supplied by the laryngeal branches of the vagus nerve (Fig. 2).

Respiration is brought about by the abductor muscles; and during respiration, the vocal cords are held apart. This is controlled by the paired posterior crico-arytenoids. These are the only true abductors of the cords. They

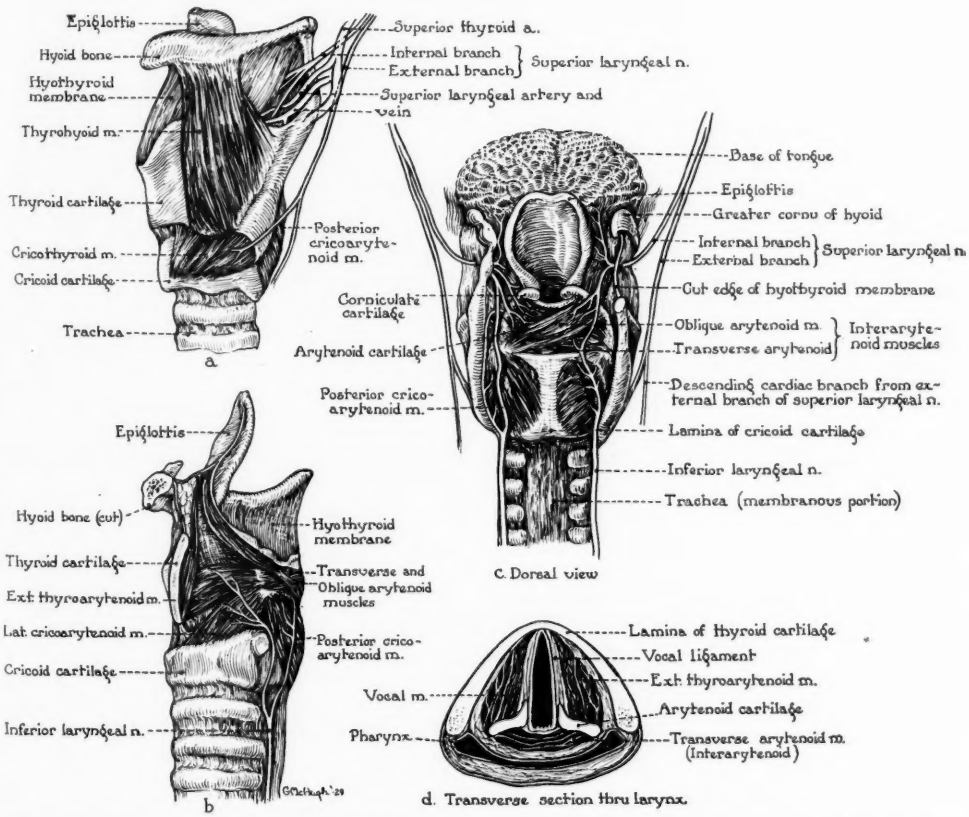

Fig. 2. Dissection of the larynx to show the intrinsic laryngeal muscles and the distribution of the laryngeal nerves (modified from Jackson). Note muscular distribution of the internal branch of the superior laryngeal nerve (permission of Surg. Gyn. & Obs.).

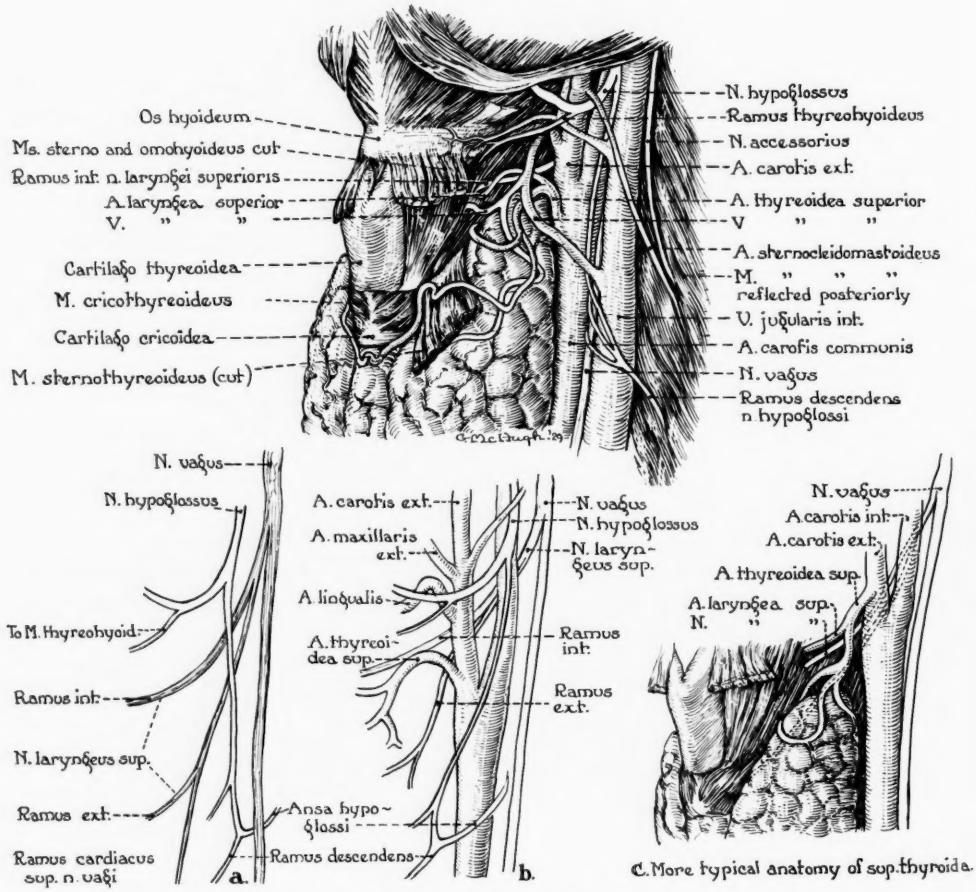

Fig. 3. Dissection to show extralaryngeal relations of the superior laryngeal nerve to the thyroid (permission of Surg. Gyn. & Obs.).

arise from the posterior surface of the cricoid lamina. The fibers (oblique and longitudinal) insert on the muscular process of the arytenoid cartilages. When these muscles contract, the vocal cords are separated.

Phonation is brought about by the adductor and constrictor muscles of the vocal cords. These muscles, when contracting approximate the cords in the midline (Fig. 2). In accomplishing this action, the lateral crico-arytenoids which antagonize the posterior crico-arytenoids, and the thyroarytenoids, which antagonize the cricothyroid, approximate the anterior one-half of the vocal cords. The posterior portions of the cords are approximated by the interarytenoid muscle. The muscle lies in the posterior aspect of the larynx and crosses the space between the arytenoid cartilages. The cricothyroid muscles (extrinsic) are composed of two distinct sets of fibers, vertical and oblique. As their name indicates, they control the change of position of the cricoid and thyroid cartilages, and when in action lengthen and tense the vocal cords. The last two muscles described are particularly important in this study because of the danger to their nerve supply (superior laryngeal).

Many studies have been made to determine the innervation of the muscles of the larynx. The internal branch of the superior laryngeal nerve is known to be sensory to the mucus membrane of the larynx. Dissections by Dilworth, New, Mullin, Berlin, Lahey and Nordland seem to demonstrate the presence of motor fibers in the nerve (Fig. 2).

From our studies of the anatomical relation of the superior laryngeal nerve, we concluded that the application of a ligature to the superior pole in a routine thyroidectomy, or in the simple preliminary polar ligation for severe hyperthyroidism, is not without danger of impairment of the functions of the larynx. The superior laryngeal nerve located a little above the outer surface of the inferior constrictor muscle of the pharynx gives off an *internal branch* which passes medially and enters the larynx through the thyroid membrane. It is mainly sensory to the larynx and supplies the interarytenoid muscle, a constrictor of the larynx by which phonation is accomplished through approximation and adduction of the vocal cords.

Whether or not the internal branch contains motor fibers, it has been demonstrated by Julian Johnson in an experimental study that injury to the superior laryngeal nerves during thyroidectomy, may be an important factor in the accumulation of postoperative tracheal mucus. Furthermore, the purely motor external branch of the superior laryngeal nerve innervates the cricothyroid muscle, the inter-

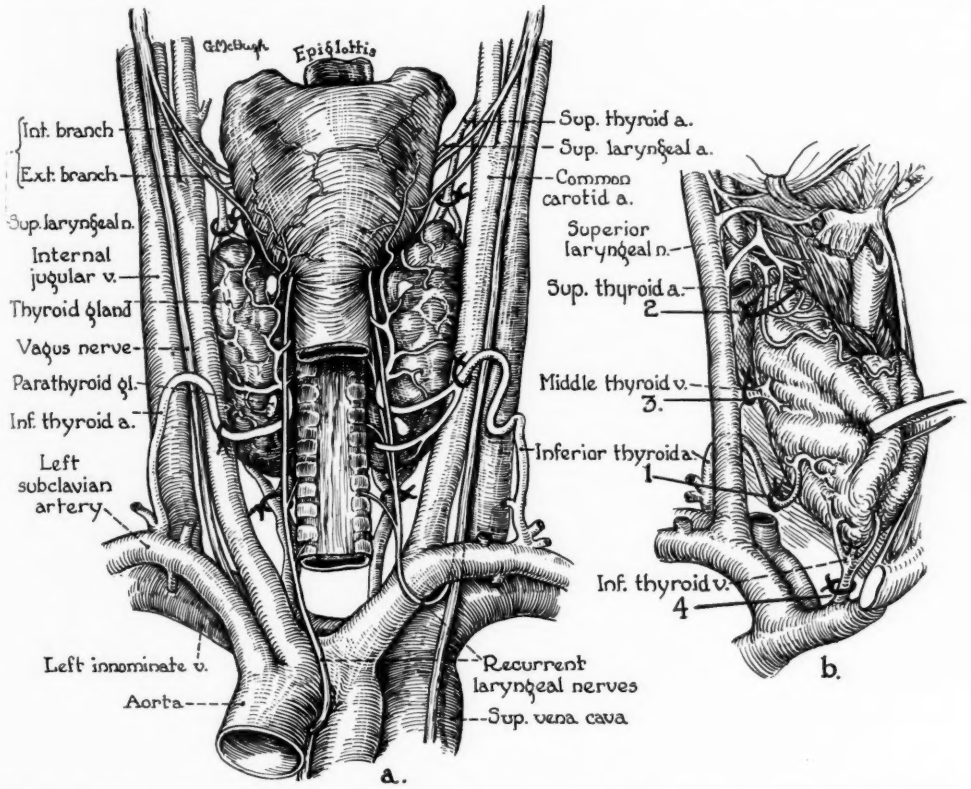

Fig. 4. Posterior view of the larynx and trachea, showing the thyroid arteries and laryngeal nerves, and the application of ligatures to the thyroid arteries to avoid the superior and recurrent laryngeal nerves (permission of Surg. Gyn. & Obs.).

ruption of which renders the voice rough, weak, and easily fatigued. For these reasons, the superior nerve must be protected (Fig. 3).

Our dissection further shows that the recurrent laryngeals arise from the vagus at different levels on the two sides—on the right as the vagus crosses the subclavian artery, and on the left as the vagus crosses the arch of the aorta. Both recurrent laryngeal nerves ascend a little lateral to the groove between the esophagus and enter the larynx at the cricothyroid articulation. A posterior view of the larynx and trachea will show the relationship of the inferior thyroid arteries and recurrent laryngeal nerves on both sides, the nerve a little farther from the tracheo-esophageal groove than usually described (Fig. 4).

Our observations clearly indicate that there are no definite differences in the relations between the inferior thyroid artery and the recurrent laryngeal nerves on the right and left sides.

As previously stated, good hemostasis is of primary importance in the surgical treatment of the diseased thyroid gland. Injury to the recurrent laryngeal nerves occurs probably most often in the attempt to apply ligatures to the branches of the thyroid arteries and in the control of hemorrhage within the capsule. The choice between the ligature of the many branches of the inferior thyroid artery intrafascially within the thyroid space, or the application of a ligature to the trunk extrafascially just after the artery emerges under the carotid sheath, should favor the latter procedure (Fig. 4). An important anatomical fact in this discussion is that the so-called external capsule of the thyroid gland is not uniformly present in the posteriomesial portion of the lower part of the gland (Fig. 5)

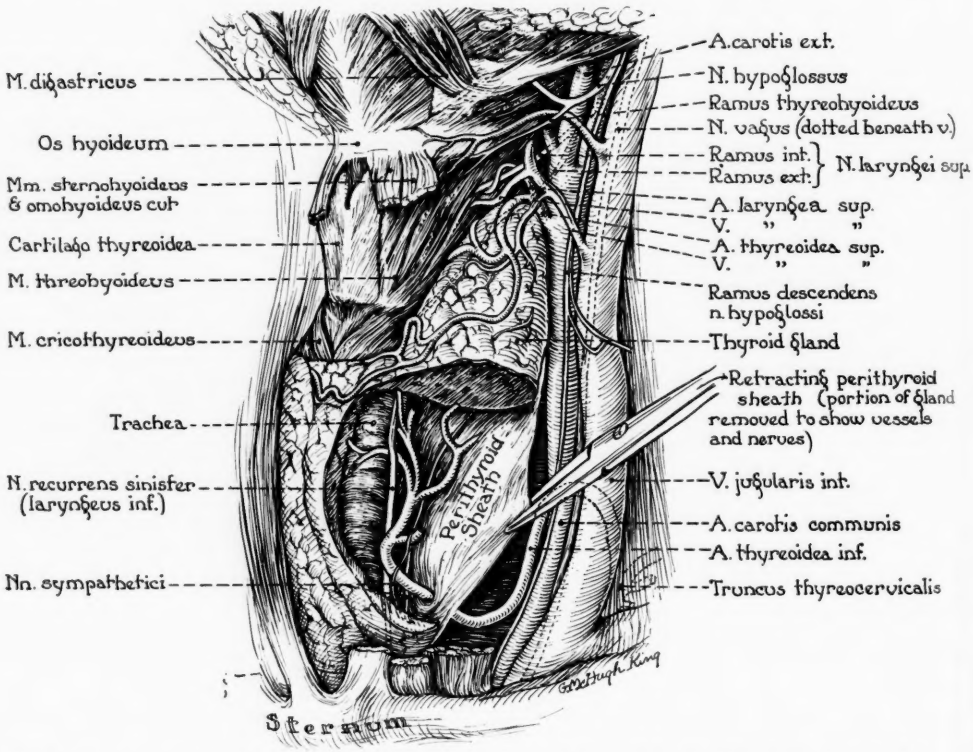

Fig. 5. Deep structures of the left side of the neck to show relations of the thyroid arteries, laryngeal nerves, and parathyroid sheath (permission of Surg. Gyn. & Obs.).

and that the recurrent laryngeal nerve is not always separated from the gland by this supposed safety zone.

The transverse section (Fig. 6) illustrates the clinical application of ligatures to the inferior thyroid artery, based on the anatomical relation. The illustration shows the usual approach to the site of the intrafascial ligation of the inferior thyroid artery, and demonstrates the danger to the recurrent laryngeal nerve in this customary procedure. In this method, the ligature is seldom applied to the trunk of the artery, but more often to one of its branches, not only endangering the recurrent laryngeal nerve, but also producing less hemostasis. The extrafascial approach for the ligature of the inferior thyroid artery, devised by de Quervain and adopted by us, is also indicated in this figure. In this method, the artery is tied at a point much farther from

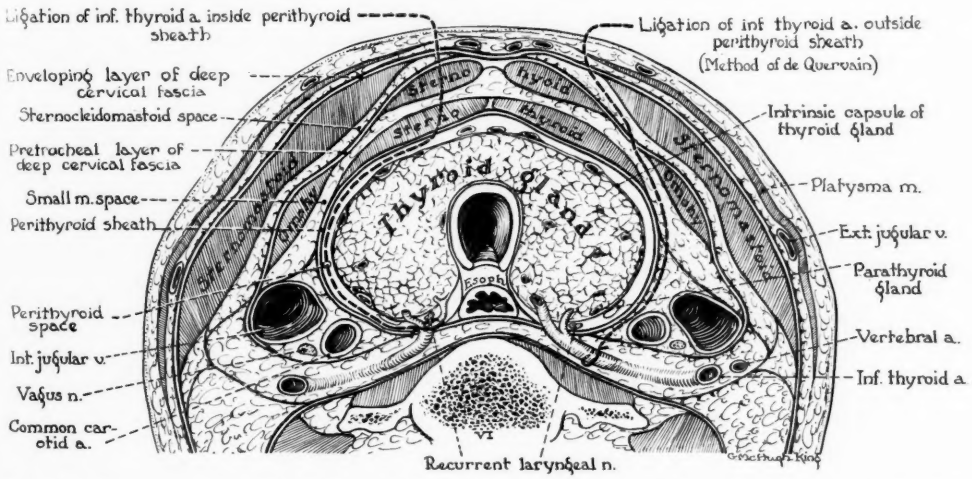

Fig. 6. Transverse section through the neck to illustrate paths of approach to the inferior thyroid artery (permission of Surg. Gyn. & Obs.).

Blocking of the principle arterial supply outside of the whole venous net work of the thyroid before the veins are interfered with, results in less engorgement of the capsule and makes delivery of the gland much easier and with less bleeding.

According to Reinhoff, preoperative affections of the laryngeal nerves occur in from five to 10 percent of cases of simple and toxic goiters; whereas, in malignant goiters the incidence is much higher. The percentage of operative injuries to the recurrent laryngeal nerves varies from one to five percent and depends to a great extent on the type of the case and the technic employed, as previously indicated. For instance, injury to the recurrent laryngeal nerve may be sustained during the mere delivery of a substernal enlargement of the left lobe, because the left recurrent nerve curves over the arch of the aorta. In a

the gland, thereby, more accurately preserving the nerve and giving more complete hemostasis. The nerve is further preserved by avoidance of postoperative hemorrhage and hematoma which might press on the nerve.

The great justification for the application of a preliminary ligature to the inferior thyroid artery extrafascially is its simplicity. series of cases of this type, there would probably be a much higher incidence of injury to the recurrent laryngeal nerve than in the ordinary cases.

The more care used in hemostasis, the less danger there is of paresis of the recurrents. Our dissections would indicate that the nerve would be more liable to injury by the intra-

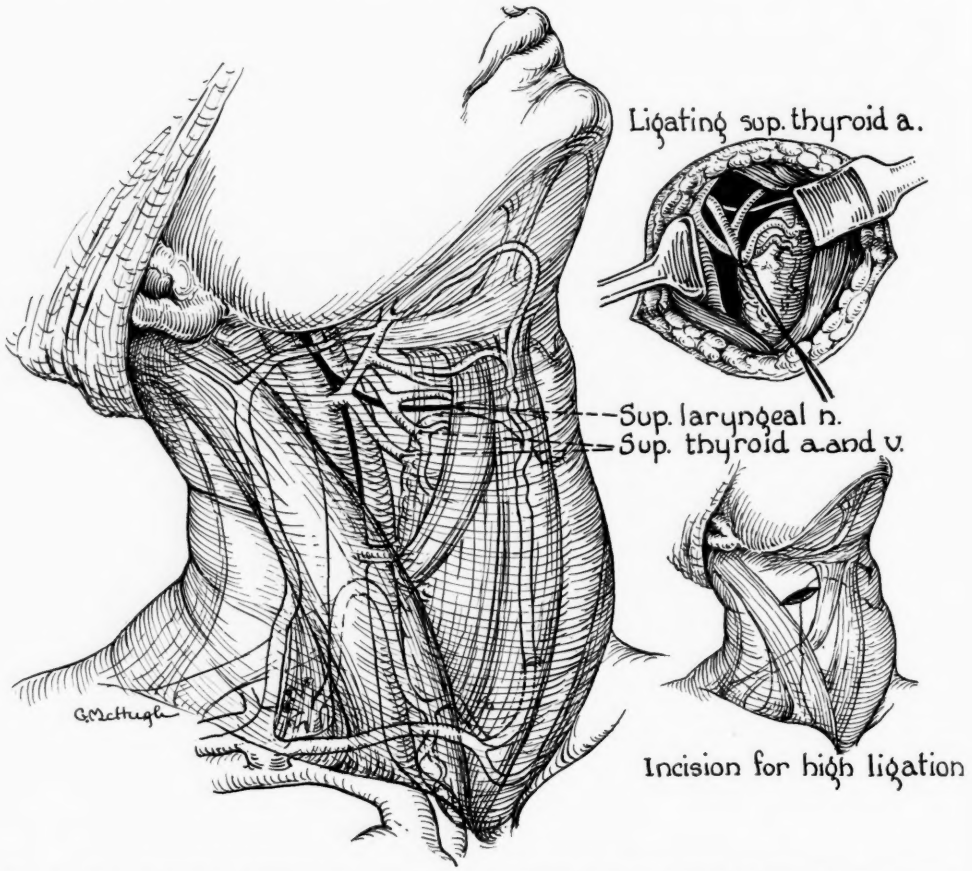

Fig. 7. *State Operation:* Ligation of superior thyroid arteries in selected cases of severy hyperthyroidism. Preliminary to subsequent thyroidectomy (permission of Surg. Gyn. & Obs.).

fascial method of ligation of the artery. According to de Quervain, injuries to the laryngeal nerves are more frequent in thyroid surgery when the gland has been previously operated upon.

Judd states that recovery of the voice usually occurs following injuries to the laryngeal nerves and dyspnea also disappears because the normally functioning cord overcompensates and approximates the affected one. Thus, the voice is restored, but usually in a lower pitch. It is probable that the percentage of injuries to the laryngeal nerves following surgery of the thyroid gland is higher than statistics show. Unless routine laryngoscopic examinations are made before and after operative procedure, one cannot be certain of the state of the function of the vocal cords. Such examinations should not be omitted.

There is a tendency to assume that with the advent of the preoperative employment of the anti-thyroid drugs, such as thiouracil, propyl thiouracil and lugols solution, that preliminary polar ligations are no longer necessary. There is no doubt but that the employment of these drugs in the preparation of patients with hyperthyroidism for operation has lessened the need for stage operations. In spite of this, there remains a place for this operation. It has previously been shown that

about five percent of patients with hyperthyroidism do not tolerate lugols solution.

Thiouracil and propyl thiouracil are not used without danger. This danger added to the economical problems involved in the long time needed for preparation must also be taken into consideration in the use of these drugs. Because of these factors, stage operations still have a place in the treatment of hyperthyroidism. Experience has demonstrated the safety and satisfaction in improvement of the patient with simple ligation of the poles (Fig. 7).

After an interval of four to six weeks, the pulse has become markedly slowed, the patient has gained weight, and all major symptoms of hyperthyroidism have receded. At this time, thyroidectomy has become a safe procedure. Until the time arrives when the use of antithyroid drugs are less dangerous than the surgical attack, polar ligations will have a place in the treatment of hyperthyroidism.

SUMMARY

In the history of thyroid surgery, the complications of hemorrhage, laryngeal nerve injury with its consequent disastrous problems and destruction of parathyroid function have been foremost in the mind of the thyroid surgeon. The surgeon should also know that he is responsible for a good functional and cosmetic result. No matter how thyroidectomy is performed, the mortality rate the world over, is now less than .05 percent. Experience has shown that a method of thyroidectomy founded mainly on an accurate anatomical approach more often results in less complications.

Besides controlling hemorrhage, the proper application of ligatures to the main arterial blood supply preliminary to thyroidectomy makes it unnecessary to apply innumerable forceps, each of which endangers the recurrent nerves. For the same reason, fewer ligatures are applied which in turn results in less drainage, a more rapid convalescence, and a greater possibility of a permanent cure.

RIASSUNTO

Le complicazioni piu' gravi che si profilano nella mente del chirurgo che si accinge alla tiroidectomia sono: emorragie, lesioni del nervo laringeo, e distruzione della funzione paratiroidea. Il chirurgo deve pure ricordare che egli e' responsaile di un buon risultato cosmetico e funzionale. La percentuale di mortalita' nelle statistiche internazionali e' scesa a meno di 0,05%. L'esperienza ha insegnato che i migliori risultati, con minori complicazioni, sono ottenuti con i metodi operatori che aderiscono piu' strettamente ai principi anatomici. L'A. richiama l'attenzione sopra l'utilita' di legare preventivamente i rami arteriosi principali: cio' non solo per prevenire emorragie, ma per evitare l'applicazione di innumerevoli pinze emostatiche, ognuna delle quali puo' danneggiare i nervi ricorrenti. La necessita' di minori legature riduce a sua volta l'uso di drenaggi, affretta la convalescenza, accresce la possibilita' di una cura definitiva.

SUMARIO

En la cirujia del tiroides el cirujano siempre tiene presente la historia de las complicaciones siguientes: hemorragia, trauma del nervio laringeo inferior, destruccion de las glandulas paratiroides, Sin embargo el es tambien resposable de los resultados funcionales y cosmeticos. La mortalidad hoy en dia es de menos de 0.5% La experiencia revela que todas las tecnicas que dependen del metodo anatomico en la reseccion de la glandula de mejores resultados con menos complicaciones. La aplicacion de ligaduras a los troncos vasculares principales de la glandula controla la hemorragia y elimina la necesidad de utilizar muchos forceps durante la reseccion de la glandula y el uso de muchas ligaduras. Esto favorece la convalescencia y la posibilidad de curacion permanente.

SOMMAIRE

Dans l'histoire de la chirurgie de la thyroïde, les complications d'hémorragie, de lésion du nerf laryngéal avec sec conséquences désastreuses et la destruction de la glande parathyroïde doivent toujours être à l'esprit du chirurgien qui opère dans ce domaine. Le chirurgien doit savoir qu'il est responsable pour un bon résultat fonctionnel et un bon résultat cosmétique. Juel que soit la méthode employeé pour la thyroïdectomie, la mortalité de nos jours et de 0,5%. L'expérience démontre qu'une méthode de thyroïdectomie

fondeé sur des connaissances d'anatomie exactes est suivie de moins de complications. Pour contrôler l'hémorragie, l'application préliminaire de ligature sur les principaux vaisseaux artériels, nous dispense de l'emploi de nombreux forceps. Nou savons que ces forceps mettent em danger les nerfs laryngés. Pour la même raison, on emploi moins de ligatures. Il en résulte moins de drainage et une convalescence plus rapide et une guérison permanente plus probable.

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Thyroid Anesthesia

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THYROID surgery can be, and too often is a treacherous affair. It thus behooves the goiter surgeon to use every device at his command to make the operation less dangerous to the patient and easier on the operator. There have been many safety factors introduced since Plummer[1] first used iodine in toxic goiter. There have been the multiple stage operations; Crile's[2] anociation technic; Lahey's[3] dissection of the recurrent laryngeal nerves, Astwood's[4] introduction of the antithyroid drugs, and many others. In attempting to make the act of thyroidectomy easier and safer, the problem of anesthesia should be carefully studied. We wish to review the different aspects of anesthesias now in common use and will try to determine which one is preferable.

Let us first consider what is the *perfect* anesthesia. Heard,[5] Cole[6] and others have various requirements for the perfect thyroid anesthesia. Combining their ideas with some of ours, the perfect thyroid anesthesia should afford goiter patients these certain safeguards.

1. It should be pleasant to take and not heighten nervous tension and therefore should be rapidly induced.
2. It should depress metabolism and not stimulate the gland.
3. It should not elevate the blood pressure and heart rate, nor cause anoxemia, nor damage the myocardium.
4. It should not increase bleeding.
5. It should not cause laryngospasm and should provide good relaxation for the removal of even large glands, yet maintain normal respiration.
6. It should be non-irritating to the bronchial tree and should not cause excessive secretion of mucus.
7. It should be followed by a postoperative period of rest without vomiting or acidosis.
8. It should have a wide margin of safety and conserve the patient's energy.
9. It should make the surgeon's task easier and the patient's ordeal safer.

Needless to say, the perfectness of an anesthesia does not lie in the drug alone, but that a great deal lies in the skill and artistery with which it is administered. In this article we hope that we can see the different anesthesias in an unbiased manner, and that we may be able to judge each—pro and con. We will attempt to omit reference to the skill of the anesthetist, in each instance only bringing out those factors which directly affect the patient and the surgeon.

LOCAL INFILTRATION

This is the old standby. A few years ago local infiltration was used by almost every thyroid surgeon and today many still use it. The original cocaine infiltration has now been replaced by less toxic agents such as novacaine, intracaine and many similar products. The patient's earnest request, "I don't have to go to sleep, do I Doctor?" promotes its usage. Some surgeons favor it for it demands gentle treatment of the tissues. The patient's speaking voice can be heard and they know when they have injured the recurrent laryngeal nerve.

The newer injectables have little toxicity both locally and to the body. It is admitted by those who use local that toxic patients are nervous, excitable and thus react poorly to the conscious state during operation under local anesthesia. This calls for heavy and accurate premedication, which practically amounts to anesthesia.

In many instances the anesthesia is not adequate, especially when the lateral lobes are elevated.[7] Thus Lahey[3] has pointed out that the surgery is definitely restricted due to a lack of proper manipulation and exposure. There is no other factor as responsible for poor surgical results as a lack of proper exposure. In attempting to deaden these pain pathways so that more exposure may be obtained, too often one finds that the minute anatomy is obliterated by the edematous tissue. Without accurate visualization of the

anatomy, serious and irreparable damage may occur.

The ever constant fear of paining the patient, of upsetting the patient, of not being allowed to manipulate as you desire add tremendously to the strain of the operator and his assistants. If strain and anxiety do shorten life, then the patient and surgeon have both lost time the day of the local thyroidectomy. Zellhoefer[8] has shown that local infiltration slows the healing of thyroidectomy incisions.

In order to retain the favorable aspects of local anesthesia some operators have used a light inhalation or rectal anesthesia to aid the local in allaying the patient's fears. These have been near perfect, yet the local may still obliterate the anatomy. The inhalation anesthesia still has its same effects, as will be discussed later.

BLOCK ANESTHESIA

This has essentially the same qualifications and difficulties as local except that the anatomy is not distorted. Most block anesthesias use adrenalin or some epinephrine like substance in the solution to prolong its effect. These are definitely contraindicated in goiter surgery.

NITROUS OXIDE

This inert gas makes a fine short inhalation anesthesia and is highly praised. The biggest, and most important objection to nitrous oxide is the anoxemia which develops when the gas is pushed far enough to get good results. Sise[9] has shown that a toxic patient who has marked, or even some, myocardial damage cannot tolerate even slight anoxemia. Barach[10] has shown how important oxygen is to the ailing heart. In all anesthetic machines there is a certain amount of rebreathing, and unless the carbon dioxide is removed adequately there will be an accumulation of carbon dioxide whose stimulating effects should be avoided.

There is considerable psychic trauma resulting from the smothering sensation experienced by the thyrotoxic patient when the mask is in place on the face. Crile's[2] anociation method of "stealing" thyroids is letting the patient breathe oxygen several mornings as if he were doing a B.M.R., then on the chosen morning he substitutes nitrous oxide oxygen mixture. This apparently limits many patient's anxiety. Recently, however, one of us asked our anesthetist to let us smell, through the same mask, pure oxygen and nitrous oxide oxygen mixture without informing us which was which. We could tell every time when the nitrous oxide was introduced and we believe that the easily excitable, nervous, supersensitive thyrotoxic patient could also detect the difference. Nitrous oxide is a weak anesthetic and laryngospasm will often occur if the anesthesia is too light. If it is too deep, then anoxemia will occur.

ETHYLENE

This gas has not found the wide use that nitrous oxide has been awarded, yet in many ways it is not unlike nitrous oxide in its advantages as well as its disadvantages. More oxygen can be used with ethylene, but it makes an explosive mixture which contraindicates the use of the electric cautery, which has proved so useful in obtaining "bone dry" thyroidectomies.

CYCLOPROPANE

Cyclopropane has many faithful followers. It has low toxicity, adequate oxygen can be used and the reaction time is rapid. Yet Lahey,[3] who uses it exclusively, states that if the concentration is a little high, cardiac irregularities are often noted, especially in the thyrotoxic individuals. This may be followed by ventricular fibrillation with sudden death.

In the toxic patient the margin of safety is quite narrow. Cyclopropane causes an increased capillary blood flow[11] with a resultant increased bleeding at the time of operation. The thyrotoxic patient needs all the oxygen carrying blood it has to help keep the load on the overburdened heart at a minimum. Cyclopropane irritates the bronchial tree to a certain extent, which should be avoided. There is an increased amount of nausea[12] and vomiting following cyclopropane which, if it occurs, may lead to several undesirable conditions such as secondary hemorrhage, change in blood chemistry, etc. Everyone is familiar with the highly explosive nature of cyclopropane and the many precautions one must take. This certainly prohibits the use of the electric cautery, which many thyroid surgeons are now finding so indispensable.

ETHER

Ether has always had the reputation of being the *safe* anesthesia, but not in the surgery of the thyrotoxic patient. It stimulates the diseased gland[5] and thus raises the B.M.R. It irritates the bronchial tree, causes an increase in the alveolar moisture, which hinders the free exchange of oxygen going into the blood stream and carbon dioxide escaping as easily and quickly as if the mucous membrane were not flooded.

Ether is usually followed by nausea, vomiting and sweating which increases the dehydration and changes the body chemistry. The vomiting and gagging tends to cause postoperative bleeding in the neck. Ether increases intracranial pressure which will in turn cause increased blood pressure and increased bleeding. Ether is certainly objectionable and unpleasant from the patient's viewpoint.

AVERTIN

Avertin is a basal type of rectal anesthesia, which is given the patient as an enema, thus it doesn't excite the patient and abolishes psychic trauma. It decreases the B.M.R. and causes a decrease in the rise of the blood pressure during the operation. These things speak in favor of its use, but as Cole[6] has pointed out, the disadvantages outweigh the advantages. It depresses respiration and encourages cyanosis. It increases the pulse rate,[13] which is already too high. More postoperative care is required and it occasionally causes nausea. It reduces the operability of the toxic patient and anesthetic deaths are more frequent than with any other agent.[6]

PENTOTHAL OXYGEN CURARE

We have discussed the usual thyroid anesthesias except pentothal oxygen curare and before we discuss the pros and cons of this anesthetic let us pause to review what it is and our manner of giving such an anesthesia, for as we said previously, there is considerable more to an anesthesia than the drug itself.

Pentothal sodium[14] is a short acting barbiturate which is not a pain relieving agent but acts as a sleep inducer, and thus its action is upon the central nervous system. Apparently the brain is the first to be affected, the spinal column next and the medulla oblongata last. The rapid action of pentothal sodium is due to the fact that it reaches the nervous system directly from the blood stream before it can be destroyed or eliminated. The exact location of the disposition of pentothal sodium after injection into the body has not been definitely determined, but apparently it is not in the liver as has been supposed in the past.[26] In large doses pentothal depresses the respiratory and vasomotor centers in the medulla oblongata. It is believed that anoxemia, if occurring, is due to decreased oxygen supply to the lungs and not due to the peripheral action of the drug. It is with this in mind that we advocate the continuous use of oxygen and we have thus come to call it pentothal oxygen curare anesthesia.

Curare is not an anesthetic agent.[15] Its main action is muscular relaxation by interrupting the efferent impulses at the myoneural junction, probably by neutralizing the action of acetylcholine.[16]

Curare is a mixture of the watery extracts of a number of plants of the stychnos species. Its activity is due to crystalline d-tubocurarine chloride. There are several types of curare. The one obtained from condrodrendron tomentosum and known as d-tubocurarine chloride affects the various muscles of the body in the following order.[16] First it affects those innervated by the cranial nerves, then those of the trunk and extremities. Thirdly those of respiration and finally those of the diaphragm. Thus optimum results are obtained if the curare in the body can be maintained at such a level as to affect the muscles of the trunk and extremities and not the muscles of respiration.

Sollmann[17] discusses another type of curare and reports the various groups of muscles affected quite differently. He fails to differentiate the different types of curare and explain them, causing comment until such is understood. The smooth muscles of the vascular system are not affected, nor does the rate, rhythm, PR, QRS or the QT interval, amplitude or configuration of the individual complexes of the electrocardiogram[18,19] show any variation.

Harris[20] reports that no change, which at present could be considered abnormal, was

observed in the electroencephalogram when curare was administered.

The contraindications to the use of curare are myasthenia gravis and the inability of the anesthetist to perform artificial respiration, which can be easily accomplished with a clear airway and the inhalation bag from any good anesthetic machine.

It is believed from laboratory experiments that curare is broken down or eliminated in about 20 minutes. This rapidity of elimination is the greatest safety factor[21] in using curare. This time element apparently is lengthened in the premedicated or anesthetized patient or in the patient receiving large or multiple doses of curare.

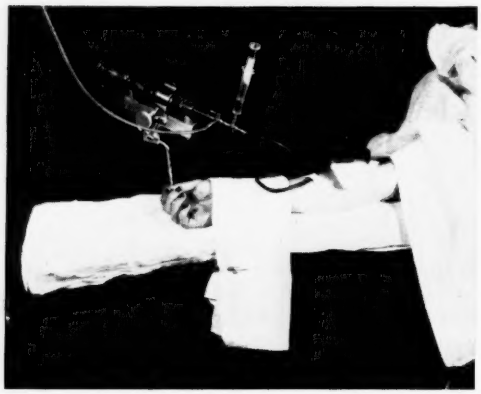

Fig. 1.

Our patients receive one and one half grains nembutal the night before operation and again two hours preoperatively, then one hundred (100 mg.) milligrams of demerol and one one-hundred and fiftieth grains (1/150 gr.) of atrophine one hour preoperatively. We use[22] the *Rudder pentothal syringe holder* to facilitate the giving of this type of anesthesia. It clamps on the arm board and holds the 50 cc. syringe, which is filled with two and one half percent pentothal sodium solution in sterile distilled water (Fig. 1). This can be injected through the short length of rubber tubing and needle into a vein (the usual one being in the anticubical fossa) by turning the knurled knobs on either side, which pushes the plunger slowly down. We usually affix a three way stopcock between the syringe and the injection needle so that a clysis may be administered through the same needle.

The patient is placed in the supine position on the operating table with the head slightly elevated. A small sandbag or rolled-up sheet is placed under the shoulders so that the neck is hyperextended, yet comfortable for the patient (this reduces the amount of neckache following thyroidectomies). The arm is placed on the arm board and the needle introduced into the vein. This procedure is done as speedily as possible, yet without flurry so as not to excite the patient. Next the pentothal solution is slowly injected and usually within 20 to 30 seconds, a minute at the most, the patient is quietly, calmly asleep. There has been no period of excitation. The oxygen mask is placed over the face and the oxygen begun. It is strongly felt that the oxygen should be started as soon as the patient has lost consciousness. More pentothal is given until the eyelid reflex is abolished. Now it is time for the neck to be prepared and draped. When this is done the patient is ready for the operation.

The anesthetist probably should now insert a metal airway to insure an adequate respiratory exchange. After placing the airway, careful attention should be made to the sound of respiration, for normal breathing has a definite character and with experience one can immediately notice a stridor which[11] would occur if one of the vocal cords were to change due to injury to the recurrent laryngeal branch of the vagus nerve. The anesthetist can then tell the operator of such change and he can at least try to find the damaged area and try to relieve the trouble.

About the time that the prethyroid muscles are being separated the anesthetist should inject 40 to 60 units of curare into the intravenous needle and allow it to be all flushed in by the clysis, which is reconnected. The acid d-tubocurarine chloride precipitates the basic pentothal if they are mixed. This precipitated pentothalic acid is quite soluble in the blood stream or in an excess of pentothal.[23] It will do no harm, but its injection into the vascular system is not desirable.

The respiratory rate is maintained between 16 and 20 for the usual patient. If the rate

becomes more rapid it usually means that the anesthetic is too light and more pentothal is needed. The relaxation of the masseter muscles shows whether the neck muscles are relaxed. Using this guide more curare can be given if necessary, usually more is not needed. In the rare instance when a patient is not deep enough and the surgeon tugs a little too enthusiastically on the thyroid the patient begins to have a little laryngeal spasm, the anesthetist should immediately give more pentothal and curare to relax this spasm. If these signs are ignored,[11] laryngospasm will occur, just as in any other anesthesia when it is too light. If the laryngospasm goes ahead and fully develops the curare still will relax it. After such an occurrence it may be necessary to hand breathe the patient with the bag of the gas machine for a few minutes to guarantee that all anoxemia be overcome. In our practice this has been a very rare occurrence.

With a little experience the anesthetist knows when and when not to give more drug. Our patients are usually lightly asleep when put back to bed. Before we started to use propylthiouracil in the preoperative treatment of toxic goiters it was occasionally necessary to "steal" a goiter. This was accomplished by having the anesthetist give the patient a gram of sodium iodide in a blue 50 cc. syringe intravenously each day for several days, then on the morning of operation substitute pentothal for the sodium iodide solution. The blue syringe camouflaged the slightly yellow pentothal solution so that the patient actually did not realize the change until she was back in her bed with her goiter out. Long and Osehner[24] and also Krump[25] have shown that the pulse rate at the end of operation under pentothal is much slower than any other anesthesia. This also has been our experience.

Thyrotoxic patients do have decreased liver reserve and it was supposed that pentothal might affect the liver, but Kohn and Apper[26] have shown that the liver is not the site of pentothal destruction. We have given this anesthetic to patients showing marked liver insufficiency with no demonstrable deleterious effects.

According to the previously stated qualifications of a perfect thyroid anesthesia let us grade pentothal oxygen curare. Pentothal oxygen curare anesthesia is safe for thyroid surgery as well as for other types of operations, as testified by our having no anesthetic deaths in over 4000 cases at the Georgia Baptist hospital, Atlanta. It is pleasant to take, and our patients don't mind having it again should the necessity arise. Pentothal is a sleep inducer, doesn't heighten nervous tension and the calm, quiet induction period is less than 60 seconds long. Pentothal depresses the metabolic rate and does not stimulate the normal or diseased thyroid gland. It does not change the blood pressure or heart rate, nor does it affect the myocardium as far as can be detected by electrocardiogram. Although pentothal in large doses does affect the medulla oblongata and its respiratory centers, if properly given, and especially if oxygen is given continuously, anoxemia does not occur. Pentothal does not increase bleeding. Pentothal and curare will relax laryngospasm already in progress (curare's only action is relaxation). It is not irritating to the bronchial tree and will not cause secretion of mucus into the alveoli. It is not followed by nausea and vomiting, but rather is followed by a drowsy feeling which sedates the anxious patient and conserves his energy.

There have been various criticisms of pentothal oxygen curare, but we have found them invariably due to a lack of information by the person making accusation or that he had experienced some bad results before he had learned to use this combination. With pentothal alone, however, some of these claims may have been justified because of the large dose required to bring about relaxation and freedom from laryngospasm and some anoxemia may have been produced. However, we feel that if our technic is followed no trouble should arise.

SUMMARY

1. The requirements for the *perfect* anesthesia for thyroidectomy have been suggested and the usual anesthesias now in use have been judged accordingly.

2. A detailed report has been made on pentothal oxygen curare and it has been illustrated how near this type of anesthesia approximates the *perfect* anesthesia for thyroid surgery.

3. The great safety of pentothal oxygen

curare has been shown in that there have been no anesthetic deaths in over 4000 cases.

4. The method of administration of pentothal oxygen curare described is greatly simplified, thus offering better control and greater safety.

RIASSUNTO

Un'anestesia veramente perfetta per la chirurgia tiroidea dovrebbe rispondere ai seguenti requisiti: essere rapida e nello stesso tempo gradevole al paziente, così da non elevarne la tensione nervosa; deprimere il ricambio basale; non aumentare la pressione del sangue e la frequenza del polso; non provocare un'anossiemia; non danneggiare il miocardio; non favorire la tendenza alle emorragie; non provocare un laringospasmo, così da conservare una respirazione normale anche allorquando si debba asportare una ghiandola molto voluminosa; non provocare un'irritazione dei bronchi ed un'eccessiva secrezione di muco; essere seguita da un periodo di riposo, senza vomito ed acidosi; avere un ampio margine di sicurezza per l'ammalato. L'A. ritiene che la combinazione di pentotal-ossigeno—curare consenta un'anestesia quasi perfetta, poiche' mentre riduce ad un minimo i rischi per il paziente, rende piu' facile il compito del chirurgo.

SUMARIO

La anestesia perfecta en la cirujia del tiroides debe de poseer lo siguiente: Debe de ser agradable y por lotanto no debe de aumentar la tension nerviosa del paciente. Debe de tener una influencia inhibitora sobre el metabolismo en general y por lo tanto no ser capaz de estimular la grandula tiroides; Debe de ser libre de efectos hipertensivos y cardio acceleradores y al mismo tiempo no favorecer la anoxemia, o la hemorragia. No debe de producir el espasmo laringeo y debe de permitir buena relajacion, sin interferir con la respiracion normal del paciente, particularmente en los casos de tamano exesivo de la glandula, Debe de ser libre de toda accion irritante del aparato respiratoria y no favorecer la secrecion bronquial. Debe de favorecer un periodo post-operatorio libre de nausea y de acidosis; debe de ser libre de todo peligro y al mismo tiempo capaz de conservar la energia del paciente; en una palabra, debe de ser capaz de facilitar el trabajo del circujano y minimizar el sufrimiento del paciente. El autor reporta el uso de la anestesia por el pentotal con oxigeno y curare y demuestra como este metodo es casi el metodo ideal de anestesia en la cirujia de la glandula tiroidea.

SOMMAIRE

Le critère, qui nous permet d'envisager l'anesthésique parfait pour les opérations sur la glande thyroïde, est le suivant:

Il faut que l'anesthésique soit agréable á prendre et qu'il n'augmente pas la tension nerveuse; par conséquent il faut qu'il individu l'anesthésie rapidement; il ne doit pas élever le métabolisme basal et ne doit pas stimuler la glande; il ne doit pas élever la pression artérielle et le train du coeur; il ne doit pas déterminer l'anoxémie ni endommager le mycocardium; il ne doit pas provoquer le laryngospasme et doit procurer un bon relâchement permettant l'extirpation même de larges glandes tout en maintenant une respiration normale; il ne doit pas irriter les muqueuses bronchiales et ne doit pas provoquer une sécrétion excessive de ces derniéres; il doit être suivi par une période postopératoire de repos sans vomissements et sans acidose; il doit faciliter la tâche du chirurgien et alléger l'épreuve du malade. L'auteur rapporte l'emploi de penthotale oxygéne curare et affirme que c'est l'agent qui approche le plus de l'anesthésique parfait pour la chirurgie de la glande thyroïde.

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Progress in Dealing with Vocal Cord Paralyses

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SINCE the first aseptic operation for the relief of obstructive dyspnea due to bilateral vocal cord paralysis which was performed in July 1938, considerable progress has been made, numerous modifications of technic have been devised, a broadened interest in the subject both by general surgeons and laryngologists has developed, and the larynx has been given a place of increasing importance in the human economy.

The results from reconstruction of the paralyzed larynx have been dramatic and in most cases, gratifying to the afflicted. With the great increase in the number of surgeons performing operations for goiter, there has occurred a corresponding increase in the number of paralyzed recurrent nerves. The need at present is for a better understanding of the anatomy of the larynx and the recurrent nerves, particularly of the relationships of those nerves to the thyroid gland, the inferior thyroid arteries and the branches of those arteries. There is also a need for better teaching of the anatomy as well as training in a technic which will reduce the number of such injuries.

The prime objectives of all operations for the relief of bilateral vocal paralyses are to secure an adequate airway and a usable voice. In general, all of the several methods employed can be grouped under one of two headings.

1. The outward displacement and fixation of the arytenoid cartilage and vocal band which is the method I devised and have used almost exclusively.

2. Arytenoidectomy with the outward displacement and fixation of the vocal cord and vocal band.

Arytenoidectomy was first performed by veterinary surgeons for the relief of dyspnea in roarer horses (due to recurrent nerve paralyses). Later the arytenoid was removed for the same reasons by a few laryngologists through a laryngo-fissure approach. It remained for Joseph Kelly[3] (New York) to popularize arytenoidectomy. His method is by cutting a small window in the ala of the thyroid cartilage on a level with the arytenoid. He then passes a small hook around the arytenoid cartilage and extracts it through the window. The vocal cord is then sutured to the muscles and fascia overlying the ala of the thyroid cartilage.

DeGraaf Woodman has modified the Kelly technic. He approaches the arytenoid from the rear by dividing the fibres of the inferior constrictor muscle and then separating the mucosa of the hypopharynx from the thyroid cartilage and a portion of the cricoid. This exposes the arytenoid which is removed. The vocal cord is then displaced outward by suture, accomplishing the same purpose as the Kelly operation. Others, including H. B. Orton, have made slight modifications of the Kelly and Woodman technics. More recently Wm. C. Thornell (Cincinnati) has removed the arytenoid by a direct vision laryngoscopic technic.

It is not my purpose to discuss the merits of the various technics. Perhaps it is best for those interested in performing the operations to concentrate on one technic and strive to perfect it.

As stated earlier, I have used the method of displacing the arytenoid outward and fixing it to the thyroid cartilage in a state of outward rotation. This technic will be described later.

The original operation was devised with, or upon the idea of a substitution of muscle function. The omohyoid was divided and attached to the arytenoid cartilage for the purpose of replacing the paralyzed cricoarytenoideus posticus. The cricoarytenoid joint develops a state simulating ankylosis in cases of bilateral cord paralysis. It was found necessary to divide the posticus and interarytenoideus muscles and disarticulate the arytenoid cartilage as well as fix it in outward displacement. Time and experience proved that it was the outward displacement and fixation which secured the results and not the transposed omohyoid.

If an adequate airway can be secured, and it usually can, by operating on one cord, it pro-

duces a much more satisfactory result than is secured by operating on both sides. The reason is that the vocal band of the unoperated cord is in the phonation position and in better condition and position for the production of sound than is the displaced vocal band. If an adequate airway is not secured by the unilateral operation, it becomes necessary to operate on both cords.

One might conclude that it would be possible to obtain an equal degree of displacement in all individuals, but such is not the case. The width of the pyriform fossae in some individuals is greater by from 3 to 5 mm. than in others. It is wider in men than in women, just as the larynx is larger in men. This difference is somewhat nullified because the arytenoid cartilage is larger in men.

The best results, as far as the combined functions of voice and airway are concerned, result when an opening of from 4 to 5 mm. between the vocal processes is secured. An opening of less than three mm. produces a good voice but inadequate airway. An opening of more than six mm. produces an excellent airway, but only a whisper for a voice. It is, therefore, important to set the opening as near 4 to 5 mm. as possible.

On a few occasions with a unilateral operation, I have secured an opening too wide. Within a few days after the operation, despite the swelling and edema in the larynx, it was apparent that these patients had secured excellent airways, but were only going to have a whisper for a voice. In three such cases, I went back and opened the wounds, cut the sutures displacing the arytenoid cartilages and placed a small piece of muscle between the arytenoid and thyroid cartilages, thus lessening the displacement with consequent narrowing of the airway. In all three, there resulted a quick and marked improvement of voice as well as an adequate airway.

The most recent advance in surgery of vocal cord paralyses is reported by Lewis F. Morrison *Annals of Otol. Rhinol. and Laryngol.* Dec. 1948, under the title of "The 'Reverse King Operation'."

This operation was performed for the purpose of restoring the voice in a man who had a unilateral cord paralysis in extreme abduction with aphonia. In his case, as sometimes happens, the unparalyzed cord was unable to develop compensation and cross the midline of the larynx to appose the paralyzed and displaced cord, creating air waste with practically no voice.

Much of the technic employed is similar to that for bilateral cord paralysis with both cords in the midline, except in the original operation the posticus muscle is cut away from the muscular process of the arytenoid, the cricoarytenoid joint disarticulated by complete division of the joint capsule, the cricoarytenoideus lateralis fibres cut and the arytenoid cartilage vocal band displaced and fixed outward. The reverse operation does just what the title indicates. It displaces the arytenoid mesially and fixes it on the midline of the posterior rim of the cricoid cartilage, thus displacing the vocal band to the midline so that the unparalyzed cord can appose it during phonation efforts. The complete technic is accurately described by Morrison. His case develoed a practically normal voice in a very short time.

I have performed the operation twice but with less success than was secured in Morrison's case. In both instances catgut was used to fix the arytenoid in position. This was a mistake. Following its absorption, the vocal band shifted outward, diminishing the strength of the voice in each case.

From the foregoing comments, it may properly be deducted that the reconstruction of the paralyzed larynx consists in placing and fixing one cord in the position of most efficacious usefulness, in regard to both airway and voice, bearing in mind that there must be a compromise between airway and voice. Only in the event of failure to secure an adequate airway and usable voice should both cords be operated upon.

I have found that the same principles may successfully be applied to a few other pathologic states in the larynx, not the result of recurrent nerve paralyses.

1. Bilateral ankylosis of the arytenoid cartilages with both vocal cords fixed in the midline.

2. Certain traumatic injuries to the larynx resulting in a fixed midline position of both vocal cords.

In the very few cases of bilateral ankylosis

of the cricoarytenoid joints which I have observed, it has been most difficult for me to make an accurate diagnosis of the condition prior to exposure of the joints, which renders the diagnosis simple. Some authors have stated that the diagnosis can be easily made through direct laryngoscopy by grasping the arytenoid cartilage with a properly designed forcep and a lack of mobility can be observed. Never having resorted to this method of examination, I am unable to state an opinion. However, in cases of bilateral vocal cord paralysis of long standing there exists a condition simulating ankylosis of the cricoarytenoid joints, I am certain as a fixed condition of the joint has been observed in practically all cases operated upon. The most distinguishing clinical feature that I have observed has been that in cases of paralysis the arytenoid cartilages come to rest in practically a horizontal position overlying the glottis resulting from a loss of tone in the paralyzed posticus muscles, while in ankylosis in the two cases I have seen, the arytenoids were in an erect or perpendicular position in relation to the vocal cords.

The operation for relief of the condition is identical to that for vocal cord paralysis with the cords in a midline position, the only difference being that it will, as a rule, be necessary to operate on both cords in order to secure an adequate airway particularly if the ankylosis has existed for a long time and is of firm fixation.

Concerning injuries to the larynx, I have only encountered one case where the technic and principles of the cord operation were applicable. In some respects it proved to be the most interesting and successful operation of the sort that I have performed. So much so that it seems worthy of detailed description.

CASE REPORT

This case report deals with a nine-year old redhead, freckle faced Irish lad. On short acquaintance, it became apparent that he possessed much more than an ordinary penchant for finding himself in difficult situations. As to what acts he committed on the occasion of his misfortune, I was not able to learn. He lived in the neighborhood with an old man who possessed an angry and irascible disposition and, who may have served as a stimulus to his unwarranted zeal and resourcefulness in the concoction of mischievous design. As to what acts precipitated the difficulty, I do not know, but it was reported that the old man emerged from his house with a 32 calibre pistol and began firing. The first bullet passed entirely through the left chest just above the heart. The second passed through the neck from left to right at the level of the cricoarytenoid joint. The great vessels of the neck were not injured. The left posterior border of the thyroid cartilage was knocked off. The posticus muscle was torn away as well as the muscular process of the left arytenoid. The interarytenoid muscle was completely avulsed. The right arytenoideus posticus muscle and recurrent nerve were not injured. The hypopharynx was opened and slit transversely. The boy was immediately taken to the hospital where a livesaving tracheotomy was performed. He was fed through a nasal tube for some time. Later his pharynx was dilated successfully and no dysphagia resulted.

Two years later I made his acquaintance. At the time, he presented small scars showing the points of entrance and exits of the bullets. He was wearing a tracheal cannula and had a moderately husky voice. Examination of the larynx revealed the vocal bands in apposition in the middle position. The left cord was completely immobile. There could be observed the tiniest bit of effort at motion of the vocal process of the right arytenoid cartilage. The arytenoid cartilages were fixed in apposition. It was concluded that the left cord was completely paralyzed but not the right, although, from examination, it was difficult to determine why the restricted motion in the right cord.

An exploratory operation was decided upon with the idea of displacing the left cord and arytenoid outward. In addition to the previously mentioned pathology, the cricoarytenoid joint was found to be completely ankylosed. It was disarticulated and the scar tissue between the arytenoids was excised and the left arytenoid surrounded by two sutures and fixed to the lateral border of the thyroid cartilage. The right arytenoid cartilage was manipulated so as to mobilize it. On the ninth postoperative day the cannula was removed. There was secured an adequate airway, the

right vocal cord had returned to almost normal excursion and he possessed a good voice. When last seen, undaunted, he was again heading for trouble.

To date, I have operated on 108 patients for bilateral cord paralysis, two for unilateral paralysis in extreme abduction with aphonia, one for bilateral ankylosis of the arytenoids with the vocal bands fixed in the midline and one for a gunshot wound with a similar type of obstruction. It hardly seems desirable to make a complete classification of the results. It may be said that all but two could converse over the phone. The tracheal cannula has been removed in all except two, one of whom could comfortably go with the cannula plugged, but on account of fear refused to have the cannula removed. The other patient could undoubtedly be relieved of the cannula by operating on the other cord. Two of the patients have taught or are teaching school; one is the secretary in a physician's office; two are trained nurses and a number of others are gainfully employed.

Lewis Morrison of San Francisco has successfully operated on 47 cases. Pemberton of the Mayo Clinic, when last seen, had operated on more than 30 cases. Hollinger of Chicago, Richard Mahon of Dallas, and numerous others have also had successful results with arytenoid displacement and fixation.

The following description of technic is, at present, routinely used and has been used for the last five years. Personally the technic herein described has proved more successful than was obtained in my early experiences with the operation when the omohyoid muscle was considered a factor of importance in securing an adequate airway. We no longer believe the omohyoid transposition to be of importance. This technic, except for minor alterations, was recently reported by Chevalier Jackson and Chevalier L. Jackson.[8]

IMPROVED TECHNIC IN THE KING OPERATION FOR RELIEF OF BILATERAL VOCAL CORD PARALYSIS

Experience has shown that the results obtained in the operation for the relief of bilateral abductor cord paralysis were not always the same when the original technic was used.[1] By a modification of that technic, described in "Diseases and Injuries of the Larynx," by Chevalier Jackson and Chevalier L. Jackson, an adequate airway was secured in a higher percentage of cases. Inequalities of voice have occurred following operation by either technic. Failure in securing a voice and airway of uniform standard is thought to be due more to inherent differences with which the surgeon is dealing than to alterations of technic. Human larynges vary in size and shape almost as much as human noses.

In the majority of patients, an adequate airway and a good voice were obtained. Considerable variation has occurred in the 108 patients studied after operation. The differences in voice range from an actual improvement in two instances to only a whisper in two. Most have some huskiness of voice.

As for airway, it may be said that an opening between the cords of less than three mm. produces an inadequate airway and one of more than five mm. will produce a poor voice although an excellent air supply. Patients learn automatically to vary and improve the airway but this is controllable only to a limited degree.

It can be stated with certainty that, following a bilateral operation for relief of paralysis of the vocal cords, the average voice will be less satisfactory than when operation is performed on one cord only. It is believed that most of the sound produced in the larynx following the operation is the result of vibrations of the undisturbed cord. Therefore the vibratory function must be preserved.

Contractures of the paralyzed vocal cords are not always of the same degree. Vocal cords vary considerably in length. The length of the cord in the male averages one and one-half times that of the cord in the female. It is easier to secure a good airway when dealing with a long cord. The larynx in the male is much larger than that in the female. The pyriform fossae of the larynx are wider in the male than those in the female. Therefore, during the operation a greater outward displacement of the arytenoid cartilage is possible in the male than in the female. Also, the width of the fossae may vary considerably in individual members of the same sex. All factors must be considered in the course of an operation. Unless one has thoroughly studied the larynges of both sexes, it is not easy to make the necessary calculations.

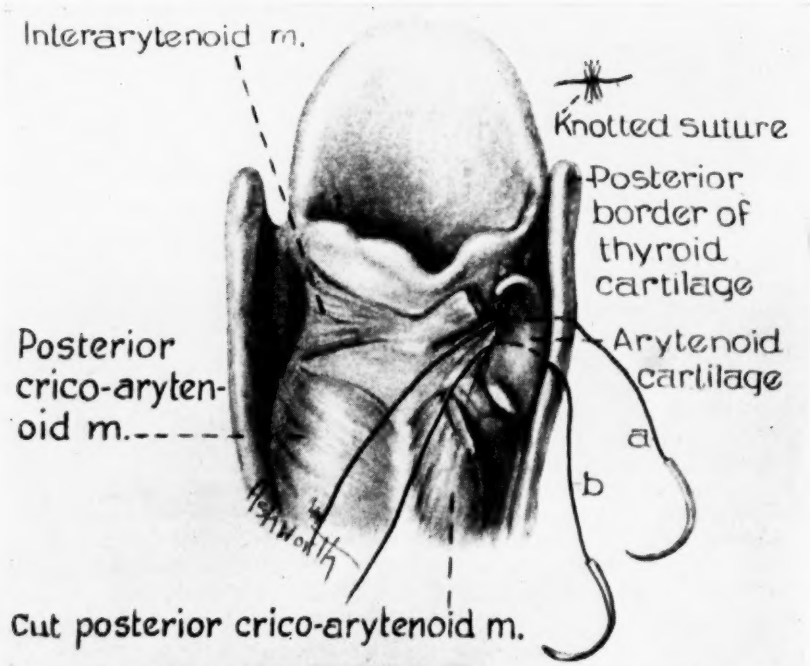

Fig. 1. This is an illustration of just what is desired to be accomplished in the operation. The crico-arytenoid and interarytenoid muscles have been divided. The crico-arytenoid joint has been thoroughly disarticulated (note joint facets). The arytenoid cartilage is displaced outward in a state of partial rotation. Note that the arytenoid cartilage is in contact with the outer border of the thyroid cartilage. This is the position which has given the highest percentage of good results. In passing the needle around the arytenoid cartilage, caution should be exercised. Hug closely to the cartilage as it is easy to perforate the laryngeal mucosa and thus infect the wound.

Physiologically, it is by outward rotation of the arytenoid cartilage rather than by outward displacement that an adequate airway is produced. Postoperative study of these patients emphasizes this point. It was concluded that a technic that would displace the arytenoid cartilage outward in a state of partial rotation would be an improvement, as any failures in the operation were the result of insufficient airway.

At first, a technic by which the arytenoid cartilage could be displaced outward and maintained in a position of partial rotation seemed difficult to achieve. However, two rather simple methods, herein described, were evolved. Both are effective but one is technically easier to perform.

Patients develop a definite capacity to widen and decrease the opening between the vocal cords. This function is thought to be due largely to the actions of the cricothyroid muscles supplemented by the suprahyoid group of muscles. Patients are also able, in some instances, to improve the quality of the voice by persistent effort. Repeated laryngeal examinations reveal that it is the undisturbed cord which develops the greater range of motion. This range seems to be due to tension and relaxation rather than abduction and adduction, though the result is somewhat the same.

TECHNIC OF COMBINED TRACHEOTOMY AND LARYNGOPLASTY

Tracheotomy is a necessary companion to laryngoplasty performed for the relief of

paralysis of the vocal cords. About 25 percent of the patients had been tracheotomized from one to 24 years. In former articles it was stated that preliminary tracheotomy should always precede laryngoplasty and muscle transportation. For the past five years or more, when the patient had not previously had a tracheotomy, I have routinely performed a tracheotomy and laryngoplasty at one sitting. The technic of the combined operations plus improvements will be described.

In patients with tracheotomy, preoperative sedation is recommended. My preference is for either 1/4 grain (0.015 gm.) of morphine or 1/3 grain (0.020 gm.) of pantopon combined with atropine 1/150th grain (0.0004 gm.). To patients on whom tracheotomy is to be performed, be it a preliminary tracheotomy or combined with the plastic operation, any sort of sedation is absolutely contraindicated. This statement holds good as regards tracheotomy done under any and all circumstances.

The combined operation can be and has been performed under local anesthesia. However, this is less practicable than general anesthesia and renders the use of the laryngoscope during the operation difficult. Pentothal sodium given intravenously is highly satisfactory as an anesthetizing agent.

TRACHEOTOMY

Before performance of tracheotomy, a syringe loaded with a solution of sodium pentothal is made ready. A needle is inserted into one of the veins at the elbow and the syringe connected to it by rubber tubing. When the tracheotomy operation has proceeded to a point where the trachea is opened and the cannula inserted, the pentothal solution is injected into the vein, and the procedure from thereon are continued under general anesthesia.

The patient's neck is prepared by any of the accepted skin-cleansing technics. My preference is soap and water, followed by alcohol, ether, and merthiolate. One percent of novocaine is then injected, infiltrating the tracheotomy area. If the patient has previously had a thyroidectomy, I prefer a transverse incision for the tracheotomy rather than a midline incision. Tracheotomy wounds are never aseptic. Transverse incision will be further removed from the laryngoplasty incision than if tracheotomy is done using a midline incision.

An incision 1½ to 2 inches long is made. Skin flaps are dissected above and below just as is commonly done in goiter operations. The fascia is opened by an up and down incision and the muscles separated. This usually exposes the trachea as in most instances the isthmus of the thyroid gland will have been removed. The trachea is opened longitudinally. The opening should begin about ½ inch below the level of the transverse incision in the skin. Otherwise when the skin is closed, the upper flap will exert pressure and leverage on the cannula with the possibility of pressure decubitus on the posterior wall of the trachea at the lower end of the cannula. One number 0 chromic catgut suture is taken in the muscles above and one below the cannula. The skin is closed with interrupted silk sutures. If the opening in the trachea is made at the proper level, the skin may be closed snugly around the cannula with no tendency for the upper flap to override. A no. five cannula for women and no. five or no. six for men should be used.

After the tracheotomy is completed, a small catheter attached to a suction tube is inserted into the opening for the purpose of removing blood or clots which may have accumulated in the trachea or bronchi. At this point a redraping of the patient is necessary. A woven wire tea-strainer is placed over the tracheotomic cannula, the mesh of the strainer having been at one point spread by a pointed hemostat. Into this opening a catheter connected to an oxygen tank is inserted. Over the strainer and tracheotomy field a sterile towel is spread, the edge of which is placed just above the rim of the strainer. Over the towel is placed a sterile 2-ft. sq. of rubber sheeting or oiled silk. Both are fastened snugly by means of skin clips to the skin above the strainer and transverse incision. This is done to prevent expired air from the tube blowing over the new operative field.

LARYNGOPLASTY

The skin above the tracheotomy area is repainted. The operating team changes gloves and gown and the patient is redraped with sterile drapes. A new set of sterile instruments is used.

An incision 2½ to 3 inches long is made over the lateral border of the larynx or thyroid cartilage. It should be parallel to and ½ to ¾ inch in front of the anterior border of the sternomastoid muscle. To a righthanded surgeon the left side of the neck will offer an easier approach. The skin and platysma muscle are incised. The superficial layer of the deep fascia and the tissue lying between the sternomastoid muscle and the lateral border of the thyroid cartilage muscles are opened. The incision exposes the anterior belly of the omohyoid muscle. When the sternohyoid and sternothyroid muscles are retracted forward the fibers of the inferior constrictor of the pharynx appear. These fibers are attached to the border and outer plate of the thyroid cartilage and must be cut. The pharyngeal mucosa is then exposed. It usually contains neither longitudinal nor circular fibers, is quite thin, and care must be exercised in separating it from the border of the thyroid cartilage, pyriform fossa, and the posterior surfaces of the cricoid and arytenoid cartilages.

There is a space of about 1½ inches along the outer border of the thyroid cartilage in which no important structure is to be encountered. It extends from the superior cornu to the inferior cornu. At the superior cornu there is danger of injury to the internal division of the superior laryngeal nerve. At the inferior cornu there is danger of injury to the external division of the superior laryngeal nerve.

When the posterior surface of the cricoid cartilage is exposed the atrophic fibers of the crico-arytaenoideus posticus are brought into view. This is the best landmark for the moment. The upper rim of the cricoid cartilage is then felt and the palpating finger slid outward on this rim or border. In the unparalyzed larynx it is easy to palpate the arytenoid cartilage, particularly its muscular process. This is not true in the paralyzed larynx, however, because the arytenoid cartilage is drawn forward by contracture into a horizontal rather than the normal perpendicular position.

If one observes the fibers of the posticus muscle and cuts them with a small sharp scalpel at a point about ⅛ inch from the upper end, the crico-arytenoid joint will be opened. This joint, like any joint that has been immobilized for months or years, will be found in a state of ankylosis. In order to mobilize it, the joint capsule must be divided completely. There is an internal lateral ligament to the joint which dips over the rim of the cricoid and is attached to the anterior surface of the cricoid. The ligament is small but strong and its division is important. The fibers of the interarytenoid muscle are then divided close to the arytenoid cartilage. A small skin-hook is passed around the arytenoid underneath the laryngeal mucosa. By this means one can gauge the amount of mobility that is established. It is desirable to cut the fibers of the crico-arytaenoideus lateralis. By so doing a greater degree of mobility is secured. Then, for a successful displacement of the cartilage, almost complete disarticulation is essential. Maintenance of the proper degree of displacement and rotation must be the object of the next procedure.

Fig. 2. This illustration shows the completed operation with the arytenoid cartilage fastened in outward position and the omohyoid muscle fixed to its muscular process. The wound is now ready for closure, which completes the operation.

Because of inequalities in the width of airways secured by the technic originally described, two modifications of it have been made. In the original procedure two sutures were passed—either through or around the arytenoid cartilage. One of these was passed through the posterior border of the thyroid cartilage and tied tightly. The other was used to fasten the omohyoid muscle to the arytenoid (that muscle is seldom transposed today). Efforts to pass a needle through the cartilage were abandoned because of the frequency with which the cartilage was fractured. The first real change in technic was described by Jackson and Jackson.[8] The procedure consisted of cutting a notch in the border of the thyroid cartilage into which the arytenoid was displaced and fixed. This technic produced a greater outward displacement of the arytenoid and uniformly secured a wider airway.

In one patient, in whom it was used, an infection developed in the wound which resulted in the infection invading the thyroid cartilage with a consequent small draining fistula which required nearly one year to heal. The functional result was not influenced by the infection. Since the antibiotic drugs have been introduced, in each instance we have dusted crystals of sulfathiazole into the wound before closure. This has reduced infections to practically zero.

As infections have occurred in a higher percentage of these operations than is ordinarily experienced in aseptic operations, and as infections of cartilaginous tissues are notoriously difficult to heal, it seemed desirable to devise a technic which would be less subject to this hazard.

From the beginning it was realized that the operation failed in one detail to conform with the normal physiology of the larynx. The normal vocal cords are opened to a larger degree by outward rotation of the arytenoid cartilages than by outward diplacement. A method of technic securing both outward rotation and displacement of the arytenoid cartilage seemed desirable. Such a technic has been devised and in all instances where it has been used, an adequate airway and a usable voice have been secured.

When the arytenoid cartilage has been thoroughly mobilized and the interarytenoid muscle divided along with some fibers of the crico-arytaenoideus lateralis, a hook is passed around the cartilage. This greatly aids the surgeon in passing a needle around the cartilage. The needle should closely hug the cartilage and not enter the laryngeal cavity. A full-curved rather strong trocar needle threaded with number 0 chromic catgut is used. The diameter of the curve of the needle should be about ½ inch. The needle should always be passed from the mesial side outward.

The arytenoid cartilage on cross section is somewhat triangular in shape. Two sutures only are passed around the cartilage. One is for rotating and displacing the cartilage; the other passes around the arytenoid and through the border of the thyroid cartilage and supplements the first stitch and holds it outward. A few inches of the tail of the upper of the two sutures are cut off and folded three times;

Fig. 3. This is a drawing of the actual appearance of the cadaver's larynx following operation. It does not truly represent the appearance of the paralyzed larynx. In the paralyzed larynx the right cord will be seen with the vocal band in a perfectly straight line and occupying a midline position. The left cord will also be in a straight line but in a position of outward displacement, but with less airway than is shown in this illustration. It is not desirable to produce an airway as great as is portrayed in the illustration. The cords in the paralyzed larynx are more rigid and therefore more difficult to displace than in the unembalmed cadaver's larynx. One should not expect to visualize a similar position of the cords to that shown in this illustration.

this makes eight strands; around these eight strands the same suture is tied. The ends of the eight strands are cut off with scissors leaving a bundle ⅛ inch in length. The purpose of this is to create a large knot which will hang in the tissues at the anterior edge of the arytenoid cartilage. The needle is then passed through the thyroid cartilage near the border. When the needle is pulled, the arytenoid cartilage is displaced outward in a moderate degree of rotation. At this point, the wound is covered with sterile gauze and a sterile towel thrown over the field. A laryngoscope is then passed and while the assistant makes traction on first one and then the other end of the knotted suture, the position of the cord and width of airway are thus observed.

It is well for the surgeon to have familiarized himself with the larynx before operation and also to observe through the laryngoscope what has been accomplished. If the laryngoscopic examination shows a satisfactory airway, the suture is tied with greater traction on the needle end. If there is doubt about having produced an adequate airway, it is advisable to go back and do a more thorough disarticulation of the crico-arytenoid joint. The second suture is the same as the first. The fibers of the inferior constrictor muscle are then sutured, the fascia and skin closed. (The suture found most fitted for surrounding the arytenoid cartilage and displacing it outward is number 0 chromic catgut, on a strong trochar pointed needle, manufactured by Davis and Geck and sold under the number P271.)

This operation was originally conceived on the theory that the omohyoid muscle would replace the function of the paralyzed crico-arytaenoideus posticus. That theory has not been well sustained. It is believed today that the transposed muscle plays a role of minor importance and that the results obtained are primarily the result of outward rotation and displacement of the arytenoid cartilage and its correspondent vocal cord.

The laryngeal ensemble is a complicated one; it is too lightly and glibly passed over in the dissecting room and in anatomies. To appreciate its physiology and disturbances in function, and particularly to correct any critical malfunction, will demand a detailed dissecting-room knowledge of its architecture, innervation, and musculature.

The technic should be practiced on the unembalmed cadaver before on the living subject.

A sufficient number of operations that involve the described technic have been performed to establish the value of the operation and experience has proved that when properly performed, an adequate airway can be assured, also a usable voice secured and the patient can be freed from the necessity of enduring a permanent tracheotomy tube.

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Technic of Thyroidectomy

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THYROID surgery has advanced from one of the most hazardous to one of the most satisfactory and safest types of surgery.

The technic of thyroidectomy depends upon numerous factors. The size of the goiter, its shape, location, toxicity, the degree of friability or degenerative processes, and finally whether there are inflammatory or malignant changes present. All these influence the various steps to be made during operations on this organ. While no two goiters are exactly alike, and no two operations can be exactly the same, the basis and fundamental principles of thyroid surgery should be adhered to in every instance.

Many goiters require very little preparation for surgery and some require none. The great majority of even the toxic goiters can be safely and adequately prepared by the conventional method of treatment. This consists of iodine, sedatives, a high caloric intake and rest.

"Experienced judgment in the preparation of these patients and the decision concerning the optimal time for operation are of equal, if not greater importance than the technical procedure. The same may be said of anasthesia and postoperative management, since without experience and judgment in these fields, a thyroidectomy, although scientifically executed, may have an unsatisfactory result. In no other field of surgery is a greater variety of skill and experience needed to obtain a good result and a low mortality."[1]

The standardized requirements for safe thyroid surgery are the following:[2]

1. A favorable pulse rate.
2. Stationary weight, or gain in weight.
3. Lessened nervousness.
4. Satisfactory aponea test.
5. Satisfactory basal metabolic rate.
6. Satisfactory morale.

The requirements listed above must be met, and it may be said that the time element is of no importance within itself, but each and every requirement must be met regardless of the time element.

The condition of the vocal cords should be known, as well as the level of the blood calcium both prior to and following the operation and this is especially important for cases of recurrences.

The conventional method of treatment for preparing toxic goiter patients seems to have stood the test of time in a most satisfactory manner. This customary routine reduces the preoperative therapy and hospitalization to a minimum and safely so, provided the judgment of the patient's condition is correct.

Where it is necessary to adopt measures further than the conventional method the antithyroid drugs may be employed under close observation. Many patients, as is well known, do not tolerate antithyroid drugs, and in such cases use of the drugs should be discontinued before harm is done.

It is well to remember that every toxic thyroid that does not respond to treatment and does not die will, if given time, have a natural or spontaneous remission. If the remission does not occur and the patient dies, the surgeon can be reasonably certain that, had he intervened with some drastic, emergency measure, he would probably have hastened the patient's death.

Finally, the patient as a whole must be considered and not merely the pulse rate, the basal metabolic rate and the like. Associated pathology is frequently present, and it must be determined whether the pathology present will influence the morbidity or the mortality.

There are various technics of doing goiters, and also various anaesthetic agents. Many surgeons are followers of two stage operations and the like. It is the author's opinion that the operator should be well acquainted with all technics. The anatomy encountered should be well understood. Frequently the surgeon will develop his own method of procedure. In the opinion of the author, each patient should be sufficiently prepared to undergo a

total thyroidectomy without undue danger. If the progress of the operation and the patient's condition warrant, then the operation can be terminated with a lobectomy, or packing and a delayed closure.

Once the patient has been satisfactorily prepared—the operation should begin. This may be carried out under either local or general anaesthesia. Many surgeons prefer general anaesthetics of various types and report good results. The author prefers local anaesthesia. As Crile stated: "Any general anaesthetic does some harm to the patient." The more toxic the patient, the more important is the anaesthetic.

With local anaesthesia, a basal anaesthetic of three grains of sodium amytal the night before and six grains of sodium amytal two hours prior to the operation, with one-sixth grain of morphine, places most patients in an ideal condition. Before the six grains of sodium amytal are administered the patient brushes her teeth, urinates, has her eyes bandaged, and is placed on the carriage on which she will be taken to the operating room 30 minutes before surgery. The carriage is so constructed that it is actually an operating table, and no transfers are necessary, either prior to or immediately following the operation. It is important that the patient understands the day before operation all that is to happen except the actual operative steps. This places the finishing touches to the patient's morale.

Three to six cc. of two percent novocaine, with or without adrenalin as indicated, are used for blocking the superficial cervical plexus at a point midway between the mastoid process and the manubrium just lateral to the sternomastoid muscle. Then following an injection of two cc. of two percent novocaine medial to the muscle at a point one-half to one inch lower than the first injection, in order to block the descending branch of the 12th nerve, which supplies the ribbon muscles. A like procedure is carried out on the opposite side. The rest of the cervical region may or may not be infiltrated with novocaine, one-half or one percent.

Most authors adequately call attention to the value and necessity of good, sound and mature clinical judgment. This cannot be replaced even in a minor way with laboratory tests. Tests should be a confirmatory precaution, not a substitute for experience and clinical judgment.

One should keep constantly in mind the complications that could arise during or following the operative procedure. These are: hemorrhage, thyroid crisis, stridor, shock, collapse, tracheaitis, pulmonary complications, cardiac complications, embolism, alimentary tract complications, serum collection, acute hypothyroidism, infection, hyperthyroid psychosis, and tetany.

The Incision: It should be as short as possible as these patients wear their scars the rest of their lives. However, inadequate exposure should not be sacrificed for the sake of comeliness. The skin of most necks stretches marvelously well, and it surely is not necessary to slit the neck from ear to ear or to make an unduly long incision. In one stroke the platysma should be divided with the skin. The bleeders, if any, are clamped and tied.

After the skin flap has been turned back or up and the lower portion turned down, the cervical fascia must be divided. This should be divided as far upward as possible and far enough downward so that the lower poles can be brought into view.

It is not necessary to divide the ribbon muscles because if the goiter is large the ribbon muscles are already stretched and can be retracted over the gland then downward and laterally, in reality assisting in the elevation of the gland itself.

During all this time the pulse is counted and recorded by a competent nurse or anaesthetist. At this particular point the pulse should have dropped a little and the patient become a little more stable.

The operator has now reached more important steps in the technic.

The proper plane of surgical cleavage must be entered. This is mandatory. This plane is between the true and the false capsule of the gland. This is the exact step that too many surgeons miss and by so doing, work with and terminate with an untidy job to the detriment of the patient's immediate well-being and effecting an unsatisfactory post-operative course. The false capsule must be preserved, as the parathyroid bodies are con-

tained therein. This will prevent tetany. The patient having met the essential requirements, the operator will next determine whether the gland itself is in the proper condition for removal. If fibrosis is present to the extent that the gland cannot be rotated easily the job will be difficult. If the lobe under attack can be rotated medially in an easy manner the job should be relatively simple.

The Larger Lobe Should be Attacked First. After rotation of the gland, the upper pole must be dissected out, clamped, divided and sutured. This may be done with hemostats or with ligature carriers passing from the medial to the lateral side protecting the superior laryngeal nerve. Then the inferior pole is clamped, avoiding the inferior laryngeal nerve. It is helpful to have the patient respond to questions at this point. Next the lateral veins are clamped. These exact steps may now be carried out on the opposite side, provided the gland is to be removed en toto.

Whether the entire gland or only one lobe is to be removed at a time, the trachea should be located at this point, clamps placed beneath the gland, not in the gland substance itself and the fibrous tissue divided. It has been abundantly demonstrated that there is adequate room between the gland and the inferior laryngeal nerves for the placing of thin clamps and the preservation of the nerves. The clamping and division of the fibrous tissue is continued until the entire gland is removed.

The pulse is still being counted each three or five minutes and recorded by a competent member of the team so that the operator at all times is aware of the pulse rate. There should be a continuous decline.

Now all the clamps are tied. No. 0 catgut is used because it is easy to work with and quickly absorbed; and, guarding against the day when an inevitable infection occurs, the neck will not have to drain until all the foreign body (non absorbable sutures) have sloughed out.

Following this technic a practically bloodless operation can be done. It is important at this point to make sure that there is not the least amount of bleeding for the reason that hemorrhage is the great complication that is capable of encouraging so many other complications, namely: crisis, stridor, shock, collapse of trachea, tracheaitis, embolism, serum, infection, psychoses, tetany.

Now saline or one-half percent novocaine may be poured in the wound and the closure begun without drainage. All tissues are approximated and sutured. The author, adopting the Crotti technic has found a subcuticular stitch very valuable for the skin closure, producing a scar that in most instances can hardly be seen. The suture is pulled out on the second postoperative day. Then the neck is bandaged and the patient returned to her room and bed, and permitted to have fluids by mouth.

Under local anaesthesia it is extremely rare for the pulse not to be better at the closure than at any time during the hospital stay. This cannot be said for general anaesthesia, for inhalation anaesthesia within itself does some harm to the patient and particularly the toxic thyroid patient.

If the proper preparation of the patient has been carried out and the operative procedure has gone along well the postoperative course should be smooth, or at least without any undue events. Even the toxic cases will be ready to leave the hospital in a few days. But when complications have ensued the matter of recovery and leaving the hospital depends upon the nature and severity of the complication (a discussion within itself). The toxic patient can frequently be ambulated 24 hours after the postoperative reaction has subsided, and the non toxic case can be ambulated even earlier; however, in the opinion of the author, nothing is gained and it may not always be wise to ambulate these patients too early.

From surveys it is thought that the mortality rate for the larger and better clinics and surgeons who have a deep interest in thyroid surgery may run as low as .5 plus percent. But if the true mortality rate were known; that is the mortality rate figuring all goiters done, no doubt, it would be appalling.

In a paper read before the Arkansas State Medical Society, April 1948, the author presented 11,536 thyroidectomies done by 12 outstanding and prominent clinics and surgeons with a deep interest in thyroid surgery. They listed 67 deaths. The author added 882 thyroidectomies of his own from one institution

(St. Vincent Infirmary, Little Rock, Ark.), consecutive cases with one death. This made a total of 12,418 cases with 68 deaths for a mortality rate of .547 plus percent. Since the above report the author has added 133 cases to the 882 above making 1015 cases for a mortality rate of a little less than one-tenth percent.

Since any death following thyroid surgery could probably be avoided if the surgeon were able to handle the case over again, the ideal goal in goiter surgery is a mortality rate of zero percent; and this is not beyond the realm of possibility for the qualified surgeon who is willing to give the time, attention and postoperative care necessary. A death from thyroid surgery should certainly be a rarity.

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Treatment of Hyperthyroidism
Especially with Radioactive Iodine

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THE treatment of hyperthyroidism or Graves' disease is in an unsettled state and will continue to be so until investigation reveals a process by which the adjustment can be made at the physiologic level of the endocrines. All methods of present treatment, surgical, anti-thyroid drugs, iodine, or radiation either external or internal, impinge on hormone production and so represent an attack on the end results of the disorder. We hope and expect that in our time better treatments will be discovered.

But let us examine the treatments now available to control a thyroid that is disordered and seems to be consuming the patient in the fire of his own metabolism.

First, we must recognize that a certain number of persons go through the cycle of the disease and by avoiding doctors they avoid treatment. The natural history of the disease seems to be one of remissions and exacerbations. In time the hyperthyroidism may burn itself out and finally the patient goes into myxedema. Few doctors have had the restraint necessary to observe the natural history of this disorder—or any other—without trying to do something to the patient. Hastening to do something for a patient is often yielding to the inordinate demands of the patient but more likely it is based on the doctor's fear of the future clinical course of the disease. One classic observation that I know of is that of the celebrated English clinician W. Hale White. During his long career in the latter part of the 19th century he followed 12 thyrotoxic persons and in his old age reported[1] that seven died on an average of three and a half years after the onset of the disease and that five lived on quite well for many years without so-called specific treatment.

Surgery was attempted in his time but it was a very hazardous procedure until 1923 when the observations of H. S. Plummer[2] established the value of iodine in quieting the disordered thyroid. It is a curious thing that iodine had been held in low repute and was an outcast for half a century from medical teaching until that simple, classic two paragraph paper of Plummer's pointed out the value of iodine in smoothing the postoperative course of thyrotoxic patients.

The profession quickly seized on iodine and proceeded to give it both before and after and without surgery to ameliorate the disease. During the 1920's much of this fundamental work on the iodine response was done in the Thyroid Clinic of the Massachusetts General hospital by Professor J. H. Means[3] and his associates. They defined the iodine response, the effective dose, the causes of failure, the frequency of the metabolic response and the several clinical results of this treatment alone or in conjunction with subtotal thyroidectomy. It is still a good means of treatment in mild forms of the disease and we still use it.

Patients with mild disease may be controlled by the daily administration of five drops of a saturated solution of potassium iodide (250 mg. of iodine). There is no advantage of iodine in any other chemical form. The basal metabolic rate falls an average of 3.6 points per day for 10 to 12 days after the institution of iodine therapy. The ratio of fall is predictable and having reached its maximum in about 12 days the disease thereafter continues at about that level, although the future course on prolonged iodine medication varies from complete disappearance of the disorder to a return of the disease, in such fury, as to necessitate a change or addition of another form of therapy.

The constancy of this response to iodine is such that where the other functional tests are not available it may be applied as a diagnostic test in cases where the basal metabolism rate is at the usual normal level or only slightly elevated.

The great boon of iodine to thyroid surgery was summarized by Boothby[4] at the Mayo Clinic in 1935. He showed how it made the gland less vascular and easier to handle, how

it reduced the need for multiple operations and introduced the subtotal thyroidectomy in which four-fifths of the gland is removed at one operation. The operative mortality dropped from four percent in 1923 to well below one percent by 1935.

In the period from 1943-1948 we have seen the medical management of this disease come to the fore. The introduction by Astwood[5] of drugs of the thiouracil series, has provided a means to adequately control the mild or moderate forms of the disease.

The predicted rate of fall of the basal metabolism rate is about one percent per day for diffusely hyperplastic goiters and much slower in nodular toxic goiters treated with thiouracil drugs. However effective this drug is, we must remember that it means continued observation and expense. The doctor has to watch for toxic reactions which occur in about two percent of patients and the patient continues to have a goiter that may even increase in size under treatment. As yet we have not learned the true incidence or time interval of recurrence after omission of the drug from patients who have been well treated. In severe disease with large goiters these drugs may be quite ineffectual.

RADIATION TREATMENT

In 1901 when Professor Henri Becquerel of Paris was carrying a small vial of radium to a lecture in London there was produced a small reaction on the skin of his belly. He was quite amazed by this and consulted his friend, Dr. Besnier and in this consultation was conceived the idea of treating tissues by means of radioactive materials.

By 1902 Williams, (Boston) was treating hyperplastic thyroids with externally directed x-rays and in 1905 Dr. Abbe (New York) reported a case successfully treated by implanting radium in a small tube directly into the substance of the thyroid gland. He is said to have received this idea of placing radium in a glass vial from the inventor, Alexander G. Bell.

From 1902 to 1934 there were many goiters treated by the external application of x-rays. Menville[6] in 1932 collected 10,541 cases of hyperthyroidism treated by 75 radiologists in the United States and Canada. Of this large group 65 percent were considered cured, 21 percent improved and 15 percent failed to respond to the treatment. Such external radiation is more effective on the non-iodinized gland.

In the year 1934 Madame Curie's daughter[7] demonstrated that certain light elements (boron, magnesium, aluminum) which had been bombarded with alpha particles continued to emit energy for a short time after the bombardment was stopped. In other words, alpha particle bombardment produced radioactive forms of these light elements. This discovery stimulated similar experiments all over the world. In Italy the physicist Fermi[8] reasoned that neutrons, because of their lack of charge, should be effective in penetrating nuclei. He was able to verify this and found that the nucleus of the bombarded atom captured the neutron, and that thus there was produced an unstable nucleus which achieved its stability only by emitting an electron. Thus the final stable nucleus became an isotope which is one unit higher in mass number and one unit higher in atomic number.

As a result of many experiments starting in 1934, radioactive isotopes of every element in the periodic table was produced. One of the first such isotopes was radioactive iodine.

The use of radioactive iodine in treating hyperthyroidism is based on two facts:

1. The natural avidity that the thyroid has for collecting iodine.

2. The release of the electron within the thyroid that sends beta rays only a few millimeters into the tissue. Beta rays act the same as x-rays. The gamma rays released probably have no effect on the thyroid.

This highly selective form of radiation therapy was started at the Massachusetts General hospital by Dr. Saul Hertz in 1941 and one year later he made a preliminary report of his experience.[9] At the same time Hamilton and Laurence[10] reported their experience from California. Hertz continued this until 1943 when he joined the Navy. In the treatment of his cases *both* radioactive and ordinary iodine were used. It fell to Professor Robley Evans and myself to carry on this work and on analysis of the situation, we felt that we could not be sure whether those patients of Hertz who had improved were responding to the radioactive iodine, the ordinary iodine, or their

TABLE I

Data on 65 Patients with Hyperthyroidism Treated Only with Radioactive Iodine (I^{130}, 12 hour half life) 1943-1946

45 gm.	Average estimated thyroid weight.
32 millicuries (14-79)	Average single effective dose by mouth.
0.45 millicurie/gm	Average single effective dose retained per gram thyroid.
6	Radiation sickness.
3 days	97 percent of radiation delivered in approximately
15*	Given second doses.
1 month	Average interval to normal basal metabolic rate.
50	Responded and continue well.
11	Resulting hypothyroidism.
3	Better, but toxic six months after treatment.
1	Died, January 1949. Autopsy—11 gm. fibrosed thyroid.
0	Recurrence of disease.
65	

* Five of these received I^{131} for their second dose; the other 10 received I^{130}.

combination. Consequently, we decided that definitive use of this new agent could be established best by a program that would cover the following five points:

1. The use of radioactive iodine alone.
2. The definition of the single effective doses—the duration of its effects—the pattern of relapse, if any, of thyrotoxicosis.
3. The production of myxedema by a single dose.
4. The observation of the histologic changes in the same gland both before and after such treatment.
5. The observation of the toxic effects of radioactive iodine.

In 1946 we reported[11] our experience in treating patients with the isotope I^{130}, which has a half life of 12 hours.

These results are depicted in Table 1 and it was then and is now our belief that radioactive iodine is another effective method of controlling hyperthyroidism. We answered the five points.

From 1946 to January 1949 we have used the eight day isotope, I^{131}, in treating an additional 100 patients with this tissue selective radiation. The results in these patients are shown in the following tables. This material comes from the United States Atomic Energy Plant at Oak Ridge, Tenn.

TABLE II

100 Patients Treated with I^{131} August 1946—January 1949

Average estimated thyroid size	50 gm.
Average single effective dose by mouth	8 MC.
Average single effective dose retained	0.11 MC./gm.

TABLE III

100 Patients with Hyperthyroidism Treated Only with Radioactive Iodine with Half Life of Eight Days, I^{131} August 1946—January 1949

Responded and continue well		
1 dose	78	
2 doses	10	
Better, but toxic six months later	10	
Treated within two months	1	
Died, myocardial infarction	1	
Operated; other treatment; recurrence	0	
97% radiation delivered in	30	days
Radiation sickness	0	
Average interval to normal BMR	2	months
Resulting hypothyroidism (2 for heart disease)	8	patients

The chief objection now raised to this radiation treatment is that its action might cause a thyroid cancer to appear in later years. In discussing the quantitative aspects of radiation carcinogenesis in humans, Evans found that the doses required to produce osteogenic sarcoma by chronic radium poisoning, lung carcinoma from breathing radon, liver sarcoma following thorotrast, and skin carcinoma following exposure to gamma rays have the following factors in common.

1. A delay of 10 to 20 years between the

begining of radiation and the recognition of malignancy.

2. A low level radiation dose maintained over a period of many years.

From this comparative analysis it seems extremely unlikely that radioactive iodine therapy that releases 97 percent of its energy into the tissues in 30 days will induce carcinoma in the thyroid or urinary excretory passages.

SUMMARY

There are five good methods to control hyperthyroidism and all of these are being used effectively.

1. Iodine alone.
2. Propyl or methylthiouracil.
3. Subtotal thyroidectomy after preparation with one or both of these drugs.
4. External radiation by x-ray.
5. Internal radiation by release of beta rays from I^{131}.

Possibly a new and more physiologic method of controlling the disease will be developed in our time, but only the test of time will establish which of these five methods is the simplest, safest, and least expensive and so the best one for the patient.

RIASSUNTO

Cinque sono i metodi per controllare l'ipertiroidismo e tutti quanti efficaci:

1. Iodio solamente.
2. Propil o metiluracile.
3. Tiroidectomia subtotale dopo preparazione dei pazienti con l'una o l'altra sostanza.
4. Irradiazione esterna con raggi X.
5. Irradiazione interna mediante liberazione di raggi beta da $I.^{131}$

Puo' darsi che altri metodi, ancora piu' fisiologici, vengano scoperti per la cura di questa malattia, ma solamente un ulteriore periodi di osservazione potra' stabilire quale di questi cinque metodi sia il piu' semplice, il piu' innocuo, il meno costoso, e con cio' il migliore per il paziente.

SUMARIO

El medico posee cinco metodos de control del hipertiroidismo.

1. El yodo solamente.
2. El propil- o el metiltiouracil.
3. La tiroidectomia sub-total con preparacion previa por uno o ambos de los medicamentos mencionados.
4. La irradiacion externa de la glandula por los rayos-X.
5. La irradiacion interna por los rayos beta del $I-^{131}$.

SOMMAIRE

Il y a cinq bonnes méthodes pour contrôler l'hyperthyroïdisme et toutes ont été employeés avec efficacité.

1. Iode seule.
2. Propyle ou méthythiouracile.
3. Thyroïdectomie sous-totale après préparation avec un ou deux de ces medicaments.
4. Radiation interne par relâchement de rayons bétas.

Probablement qu'une nouvelle méthode plus physiologique pour contrôler cette maladie sera développeé sous peu, mais seulement le temps nous dira la quelle de ces cinq méthodes est la plus simple, la plus sûre et la moins coûteuse. C'est à dire la meilleure les malades.

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Pre and Postoperative Care of the Patient with Hyperthyroidism*

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CAREFUL pre and postoperative care of the patient with hyperthyroidism is imperative if restoration of normal function is to be accomplished. Here, as much as any place in surgery, the internist and surgeon cooperate closely, both before and after the necessary surgical procedure is carried out. As soon as the patient enters the clinic for examination, the internist and surgeon work together to evaluate the patient's general condition, decide on the preoperative treatment necessary, the date of the operation and the postoperative care, including care of any complications that may arise. It is important that the patient and the relatives understand fully the condition which the patient has, the reasons why surgical intervention is necessary and the future prognosis of the patient.

Operative Risk: It is the practice of Mason and Zintel to classify each patient with hyperthyroidism with regard to operative risk prior to instituting preoperative treatment. Among the factors they take into consideration in the grading of operative risk at the time of entry, are duration of the disease, age of the patient, loss of weight, pulse rate, pulse pressure and history suggestive of episodes of crises or cardiac complications. After examination of the patient by the internist, the necessary laboratory procedures are ordered and a consultation held with the surgeon, as well as with any specialists that are indicated because of liver, cardiac or other complications the patient may have. A routine laryngoscopic examination as suggested by Pemberton and his associates is always carried out.

PREOPERATIVE PREPARATION AND CARE

Rest and Recreation: During the course of the physician's discussion with the patient concerning the disease which he has, the necessity for adequate physical and mental rest is repeatedly emphasized. The physicians and nurses soon realize that such patients are easily upset by minor irritations. In addition to adequate sleep and rest, the patient should be encouraged to partake of recreation that requires only minimal physical and mental effort.

Fluids: Most patients with hyperthyroidism are thirsty and therefore will require little urging to insure an adequate fluid intake by mouth of at least 3000 cc. daily. More fluids are required if there is diarrhea, undue sweating, nausea, emesis or elevated temperature. If the patient cannot take the necessary amounts of fluids orally, five percent dextrose in distilled water or a ten percent solution in the case of the markedly toxic patient are given, inasmuch as the carbohydrates are of definite benefit. In the severely toxic patient who does not have a good response to preoperative preparation, a 1000 cc. blood transfusion may prove beneficial.

Nutrition: If the patient is to gain or maintain weight during the preoperative period, Mason, Zintel, Lahey and the great majority of others in this field prescribe additional food according to the elevation of the metabolic rate. For example, a man with a metabolic rate of 50 doing a moderate amount of muscular work requires 6000 calories daily to maintain his weight. This is the reason why thyrotoxic patients who carry out manual labor always show striking undernutrition.

Lahey and his associates keep daily weight and basal metabolic graphs on all patients with hyperthyroidism and consider a gain in weight as one of the best indications of improvement. Ordinarily, tea, coffee, tobacco and alcohol are not allowed.

It is now accepted that the liver is damaged in many patients that have hyperthyroidism and in some instances jaundice has been noted. If there is clinical or laboratory evidence of liver damage, Ravdin has found that the liver can be improved in function by a

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From the Lovelace Clinic, Albuquerque, N. Mexico.

high protein (25 percent), high carbohydrate, low fat diet.

Boothby, Mayo and Lovelace have advocated the routine administration of high concentrations of oxygen postoperatively in hyperthyroidism when there is any liver damage with its attendant sensitivity to even minimal anoxemia. For the same reason, when gas anesthesia is administered, it should be given with a high concentration of oxygen.

On the basis of Means' observation that cardiac manifestations occurring in patients with hyperthyroidism resemble those that occur in patients with vitamin B_1 insufficiency, vitamin B_1 and the B complex are given before and after surgery. These patients receiving vitamin B_1 therapy have improved more rapidly prior to surgery than those who did not as was the experience of Mason and Zintel. The average dose is riboflavin 10 mg., thiamin 20 mg., nicotinic acid 20-30 mg. and ascorbic acid 100-150 mg. a day.

OPHTHALMOLOGIC CARE

When the patient has exophthalmus to such a degree that it is impossible to completely close the eyelids, goggles which have no ventilation are often worn, thus keeping the eyes moist. This is accompanied by two to three drops of Ringer's ointment in each eye, four to five times a day. The same procedure is followed postoperatively. The Ophthalmologic Section is responsible for the eye care of these patients and carries out a detailed pre and postoperative examination.

Iodine: On the basis of the work begun by Plummer in 1923 each patient is given 10 minims of Lugol's solution three times daily. Improvement is evidenced by gradually diminishing irritability, restlessness, nervousness, tremor and tachycardia. Means has found that the basal metabolic rate fell 3.7 points each day in those patients that responded well to iodine therapy. Patients are given iodine at least 10 days prior to surgery and some patients may require it two to three weeks prior to surgery before they are ready.

Propylthiouracil: At present our use of propylthiouracil prior to surgery is confined to those patients that would otherwise require stage operations because of unusually high basal metabolic rates, very large glands and poor operative risk. These patients comprise approximately 10 percent of cases that require surgery.

The average dose of propylthiouracil is 100 mg. t.i.d. Approximately 25 percent of patients require 400 mg. a day and one patient has required 700 mg. a day. It has been possible to reduce the basal metabolism to about + 10 or below with this regime, as reported by Lahey, and for this reason operation is not carried out until metabolism has reached normal levels. Two weeks prior to contemplated surgery, the patient is started on Lugol's solution in an effort to decrease the technical difficulty that would otherwise occur at the time of surgery.

Radioiodine: Our experience with the therapeutic use of the radioactive isotope of iodine, I^{131}, has been too short for us to make specific recommendations. Certainly, we are in agreement with Haines, Keating and their coworkers that I^{131} has its most important potential use in those patients with serious complications which are due either to prolonged hyperthyroidism or to associated diseases and in those in which exophthalmic goiter tends to recur repeatedly after treatment with antithyroid drugs or surgical treatment.

Haines and his associates record that an average dose or more than 200 microcuries per gram of thyroid tissue should be tried in cases in which an attempt is made to control the disease in a single dose. There is a wide variation in the sensitivity of different thyroid glands to radiation, and so far the incidence of both myxedema and of recurrence of exophthalmic goiter after treatment is much higher among patients treated with I^{131} at the Mayo Clinic than among patients treated surgically there.

Soley and Miller also feel that clinical judgment has been the most important factor in deciding what dose of I^{131} to use and feel that studies of the problems of dosage, measurement of radioiodine and distribution of radioiodine in the thyroid are necessary, before conclusions can be drawn as to the place of this type of therapy in the treatment of Grave's disease. Keating recently stated that it is difficult to determine the dose of radiation received in an individual case as this depends

upon the weight of the thyroid, its rate of iodine turnover and the energies of isotopes employed.

At present we are studying the deposition and disappearance of radioiodine by placing a Geiger-Muller Counter over the gland, the penetration of gamma rays of I^{131} making such counting possible. Other investigations in the use of radioidine will be carried out, including their use in the treatment of adenocarcinoma of the thyroid gland.

Immediate Preoperative Orders: Inquire as to upper respiratory infection.

Soapsuds enema the night before surgery.

Nembutal, gr. 1½, the night before and the morning of surgery.

Make certain no drug idiosynerasy exists.

Nothing by mouth on the day of operation.

Morphine sulfate, gr. ⅙, and atropine sulfate, gr. 1/150, on call to surgery.

POSTOPERATIVE CARE

Position in Bed: A semi-sitting position makes it easier for the patient to swallow and breathe and permits better rest.

Tracheotomy trays should be available on the floor.

Sedation: Morphine, gr. ⅙ to gr. ¼, is given every three hours as necessary.

Nembutal, gr. 1½, can be used to promote sleep.

Patients with hyperthyroidism often have increased tolerance for morphine.

Oxygen: For the patient who has had a very toxic goiter, the routine use of oxygen in high concentrations by means of the B-L-B oxygen mask (Boothby-Lovelace-Bulbulian), or if the weather is warm an oxygen tent, is indicated, as it will decrease the respiratory minute volume, decrease the pulse rate and increase the oxygenation of the blood.

The effects of acute oxygen want that should be watched for are: errors in judgment, mental confusion, inability to concentrate, clouding of thought process and memory, restlessness, lassitude, headache, diminished night vision and dimming of vision, tremor of the fingers, elevation of temperature, pulse and respiration, and cyanosis of the lips which can be detected when the oxygen saturation of the hemoglobin is 90 percent and is definite at 85 percent. A patient with anemia may not be cyanotic even if the saturation of the arterial blood is as low as 60 percent. Frequent and shallow breathing in shock is a symptom of which the serious import is often not realized. When anoxia is present in shock which is due to other causes, it is always a contributing factor, and it may facilitate the establishment of a vicious cycle of events leading to general collapse. Anoxia itself, even in its early stages, may produce vasomotor collapse in some individuals.

Fluids: Forty drops of Lugol's solution are given in the first proctoclysis in 500 cc. of tap water. In addition, 1500 cc. of five percent dextrose in saline are given intravenously.

As soon as the laryngoscopic examination is carried out and the cords are found to be normal, cool water may be taken by mouth. If there is nausea or emesis, intravenous administration of fluids is continued so that the patient will receive 1000 cc. over the measurable output in 24 hours.

Iodine: Ten minims of Lugol's solution in fruit juice are given three times a day.

Diet: A liquid diet is given second day after surgery, a soft diet is given on the third day and a high carbohydrate, high protein diet thereafter.

Oral Hygiene: Oral hygiene for patients not taking fluids can be accomplished by using orange or lemon slices, lemon and glycerin mouthwash, frequent alkaline mouth rinses and the application of vaseline to the lips.

Care of the Wound: The wound is first dressed at the end of 24 hours, the sponge rubber pressure dressing removed. If a drain has been inserted, it is removed at this time if the amount of drainage is small and the next day if there has been a moderate amount of drainage. The nylon 0000 monofilament skin sutures are removed on the fourth day. If serous drainage is present underneath subcutaneous tissues, it can often be aspirated with a small gauge needle attached to a syringe.

Out of Bed: If the patient is in reasonably good condition, he is allowed out of bed on the day after surgery, otherwise the second day after surgery, and he is usually dismissed from the hospital on the fifth day after surgery.

Supervision After Leaving the Hospital:

The Lugol's solution is continued for one to two months, at the end of which time the patient is re-examined and the basal metabolic rate determined. If examination is essentially normal, the iodine is discontinued. The patient is examined at two to three month intervals during the next year.

The patient is warned about the possibility of a relapse if he does not take good care of himself and especially if his previous environment has been responsible for the development of hyperthyroidism.

POSTOPERATIVE COMPLICATIONS

Hemorrhage: If hemorrhage occurs after subtotal thyroidectomy, it almost always results in respiratory obstruction caused by an accumulation of blood beneath the pre-thyroid muscles. This, in turn, results in difficulties in breathing and dysphagia. If hemorrhage occurs it is necessary to take the patient to the operating room and isolate and ligate the bleeding vessel.

Tracheitis: The trachea is often irritated after thyroidectomy as evidenced by the patient's frequent attempts to clear the throat and occasionally by the presence of hoarseness, cough, dyspnea and very tenacious mucous.

Treatment of tracheitis is best accomplished by inhalations of steam and the ingestion of warm fluids. If edema of the larynx progresses, tracheotomy may become necessary.

Thyroid Crisis: Treatment of thyroid crisis consists in the administration of high concentrations of oxygen, ice packs, morphine, nembutal to control restlessness, administration of ten percent dextrose in distilled water and iodine by rectum intravenously or by hypodermoclysis. Transfusion of whole blood may be beneficial.

Tracheal Obstruction: Tracheal obstruction can result from collapse of the trachea, pressure on the trachea from hemorrhage or, most often, as the result of injury to the recurrent laryngeal nerves. If as much as possible of the operation is carried out under local anesthesia, and if the patient is routinely awakened during subtotal resection of lobes on both sides, damage to both recurrent laryngeal nerves is impossible for all practical purposes.

Treatment of tracheal obstruction is by relief of the causative factor. If measures to accomplish this are not immediately successful, tracheotomy is performed, after first giving helium and oxygen therapy a therapeutic trial.

Parathyroid Tetany: The earliest manifestations of parathyroid tetany are usually tingling and stiffness in the feet and hands and numbness of the tongue, twitching of the face and beginning contraction of the fingers.

The more severe forms of parathyroid tetany are characterized by contractures of the hands in the accoucheur's position, convulsions, laryngeal spasm and rapid respiration. Chvostek's sign and Trousseau's sign are usually positive.

The treatment of parathyroid tetany in the milder forms consists in the administration of two to four grams of calcium lactate in hot water every two to four hours. Cod-liver oil, two to three teaspoonfuls daily, is helpful in promoting the utilization of calcium. Viosterol may be given for the same purpose. If the parathyroid tetany is very severe, five cc. of a 10 per cent solution of calcium chloride or calcium gluconate in 100 cc. of normal saline solution is given. Depending on the level of the blood calcium, parathyroid extract, 10 to 50 units once daily, can be given intramuscularly.

Albright and his associates have concluded that a more sustained rise in the blood calcium level can be brought about by the administration by mouth of dihydrotachysterol (this is also known at A.T. 10).

SUMMARY

Careful pre and postoperative care of the patient with hyperthyroidism is imperative if restoration of normal function is to be accomplished. Here, as much as any place in surgery, the internist and surgeon cooperate closely, both before and after the necessary surgical procedure is carried out. As soon as the patient enters the clinic for examination the internist and surgeon work together to evaluate the patient's general condition, decide on the postoperative care, including care of any complications that may arise. It is important that the patient and the relatives understand fully the condition which the patient has, the reasons why surgical intervention

is necessary and the future prognosis of the patient.

RIASSUNTO

Nei pazienti affetti da ipertiroidismo e' necessaria un'accurata cura pre- e postoperativa se si vuole ristabilire una normale funzione della tiroide. Come in qualsiasi contingenza operatoria, anche quì si rende necessaria prima e dopo l'operazione un'intima collaborazione fra il chirurgo e l'internista. La collaborazione incomincia dal momento in cui l'ammalato consulta la clinica, onde valutare le condizioni generali di salute, decidere le opportune misure preoperative, stabilire la data dell'operazione e prospettare le cure postoperative nell'evenienza di complicazioni. E' bene che tanto il paziente, quanto i famigliari, siano resi pienamente edotti della natura della malattia, delle ragioni che richiedono l'operazione, della prognosi.

SUMARIO

El tratamiento pre y post-operatorio del paciente con hipertiroidismo es de suma importancia si se quieren obtener restauracion completa de las funciones normales del paciente. En esta enfermedad es imperativo la cooperacion completa del internista y del cirujano, tanto antes, com despues de la cirujia. Entre los dos esta la responsabilidad de decidir el tratamiento pre-operatorio, la fecha mas favorable para la operacion, y el regimen post-operatorio, incluyendo el tratamiento de las complicaciones que se presenten. Tambien es de importancia el explicar al paciente y a la familia de el, su enfermedad, las razones para la operacion y el prognostico post-operatorio y en el futuro.

SOMMAIRE

Le choix des soins pré et postopératoires donnés aux malades souffrant d'hyperthroïdisme est très important si l'on veut obtenir une restauration complète de la fonction normale. Ici, comme dans beaucoup d'autres conditions chroniques, il importe que le médecin et le chirurgien s'entendent avant et après le procédé opératoire indiqué. Aussitôt que le malade est admis à la clinique, le médecin et le chirurgien travaillent ensemble afin d'évaluer l'état général du malade et de décider sur le traitement préopératoire approprié, la dâte de l'opération, le traitement postopératoire et aussi les soins de toute complication qui peut survenir. Il importe que le patient et sa famille soient renseignés l'état du malade, les raisons pour lesquelles une intervention chirurgicale est nécessaire et le pronostic futur du malade.

Preoperative and Postoperative Treatment in Hyperthyroidism*

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FOR several decades the most satisfactory treatment for hyperthyroidism, whether due to a toxic diffuse or a toxic nodular goiter, has been a bilateral subtotal thyroidectomy. During recent years with the advent of radioactive iodine and the antithyroid drugs, the indications for operation are much less absolute. This is particularly true as regards toxic diffuse goiter in which operation has by no means been a completely satisfactory procedure. Opinion as to the method of treatment of toxic diffuse goiter varies from that of those physicians who believe that all patients should be treated for cure by medical means to those who still think that all patients should be treated by surgical means. Most physicians agree that all patients with toxic nodular goiter should sooner or later have their goiters removed. Without entering into this controversy, and solely for the purpose of discussing pre- and postoperative treatment, let us assume hypothetically that all patients with thyrotoxicosis are to be subjected to a thyroidectomy.

After Plummer[25] in 1923 introduced iodine in the preoperative treatment of hyperthyroidism the method of treatment was fairly well standardized for two decades. It consisted essentially of (1) administering iodine as Lugol's solution in doses of five to 10 drops three times daily, (2) a high caloric diet and (3) partial rest. Such treatment gives a noticeable and prompt amelioration of symptoms in toxic diffuse or exophthalmic goiter. Treatment was continued as long as the patient continued to improve and when improvement ceased, usually after a period varying from three to eight weeks, he was operated upon. Depending upon his general condition a unilateral or bilateral subtotal resection was performed. The same preoperative treatment does not produce similar striking improvement in the symptoms of toxic nodular goiter. Indeed, improvement is of such little moment that most surgeons prepared the patient by the above means for only two or three weeks and operated upon him regardless of the severity of the disease or his general condition. About all that one could do was to remedy the effects of undernutrition or congestive heart failure and accept the surgical risk whether it were good or bad.

One could, by various criteria, estimate the surgical risk rather accurately but in adverse circumstances little can be done to diminish the risk other than pay meticulous attention to the operative and postoperative details. Thus Plummer's epoch making contribution, sharply reduced mortalities in toxic diffuse goiter but had little effect on the mortality of thyroidectomy for toxic nodular goiter except in so far as the general reduction in death rate influenced patients to submit to operation before damage was too great. These factors reduced mortality rates after 1923 from somewhere between six to 10 percent down to between one and three percent.

The second epoch in the care of the thyrotoxic patient began with the following: experimental evidence of Mackenzie and Mackenzie[21-22] that sulfaguanidine inhibited the production of thyroxin in the rat; the observations of Kennedy[16] of the goitregenic effect of allylthiourea; experiments of Richter and Clisby[26] on the similar action of phenylthiocarbamide. The evidence was completed by the brilliant experimental and clinical investigations of Astwood[1] on the effectiveness of thiouracil.

When Astwood[2] later introduced propylthiouracil, a drug of lesser toxicity, the use of the antithyroid drugs in preoperative treatment became firmly established although by no means uniformly applied. A discussion of the preparation of a thyrotoxic patient for operation now revolves itself largely around the use of the antithyroid drugs. Hence, a

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cursory survey of the present status of this problem will be presented under the indicated sub-headings.

Choice of Drug: For all practical purposes only three drugs need be considered, namely, propylthiouracil, methylthiouracil and thiouracil. Of these propylthiouracil is the safest. Thiourea,[29] thiobarbital[3-19] and aminothiazole[29-20-23] are much too toxic. Thiouracil administration carries a reaction rate of 12 percent or more.[28] Barfred[5] reported 61 cases treated with methylthiouracil with a reaction rate of 12 percent and made a collective review of 604 cases in which he found that seven percent had toxic reactions severe enough to discontinue treatment and 11 percent had mild reactions not interfering with therapy. This is considerably higher than the three to six percent incidence of reactions following propylthiouracil therapy.[2-4-13-19]

Although propylthiouracil is at present the preferred drug it will undoubtedly be replaced by a better one. Stanley and Astwood[27] have tested the relative activities of a number of antithyroid compounds in man by calculating the diminution of the uptake of radioactive iodine in the thyroid and by this method have found a number of compounds of greater potency than propylthiouracil.

Their previous methods for the evaluation of the potency of the antithyroid drugs have depended upon the goitregenic action of the drugs in the immature rat—an increase in the weight of the gland plus a depletion of iodine. The disadvantage of this method of assay is uncertainty that the results obtained will be applicable to men. By this method of assay Astwood found that propylthiouracil was 11 times more active than thiouracil, but by the assay with radioactive iodine in man, he found the two drugs to be of approximately equal potency—a finding more compatible with clinical observation. On the other hand, by this method they found several drugs more active than propylthiouracil and one, 2-mercaptoimidazole, which had 10 times the potency.

Dosage of Propylthiouracil: The original dosage of 75 to 150 mg. daily recommended by Astwood[2] for reasons stated above have been found to be much too small. An excellent analysis of dose has been made by Hibbs and McCullagh.[13] They found that in amounts of 150 mg. or less per day the drug was ineffective in 42 percent of patients; in amounts of 200 mg. daily it was ineffective in 12.6 percent but with 300 mg. a day it was ineffective in only 3.7 percent. They recommended initial treatment of 300 mg. daily, as 100 mg. three times daily, and do not hesitate to use 500 or 600 mg. daily if necessary. Most investigators have come to about the same conclusion. Most certainly an initial dose of less than 200 mg. daily is inadvisable.

Reactions: The incidence of reactions is no more than five or six percent.[2-4-13] They consist of: a generalized pruritus or an urticarial rash or even an exfoliative dermatitis; arthralgia; parasthesia of the extremeties; anorexia; nausea and vomiting; fever; leukopenia. Cutaneous manifestations are the most frequent but often not severe enough to discontinue treatment entirely. Mild degrees of pruritus are of little significance. If a rash appears the drug may be discontinued for a few days and when the rash disappears it can be cautiously readministered.

Agranulocytosis, although uncommon, cannot be ignored. I have observed two patients with an agranulocytopenia and hyperpyrexia, one in the early weeks of treatment and the other after nine months of continuous therapy. It is advisable to do a white blood count weekly and if it falls below 5000 per cm. a differential count is mandatory. A relative leukopenia is not infrequent but usually a differential count reveals a normal percentage of polymorphonuclear leukocytes.

Under such circumstances treatment may be continued but if the patient is in reasonably good condition it is probably less disturbing to all concerned to discontinue the treatment and to do the operation. Judging from the reports in the literature and my own experience it can be estimated that two or three patients out of a hundred will be unable to take the drug.

Duration of Treatment: Bartels[4] has calculated that under propylthiouracil therapy alone the basal metabolic rate drops 1.3 points a day in toxic diffuse goiter and .64 in toxic nodular goiter. Hibbs and McCullagh[13] calculated the fall of the basal metabolic rate in toxic diffuse goiter at 2.95 percent per week.

These figures present only a general idea of expected improvement and are not at all reliable in estimating the duration of treatment necessary to return a patient to a euthyroid condition and treatment should, if at all possible, be continued until the patient is quite normal.

The drug is more quickly effective in a patient with a small toxic diffuse goiter and least effective in an elderly individual with a large toxic nodular goiter. In the former instance a normal basal metabolic rate may be obtained in four to eight weeks, in the latter it may require six to nine months. It is unfortunate that its effectiveness is the least where one needs it the most.

The highest surgical risk is in patients past 60 years of age with toxic nodular goiters and it is in exactly these patients that amelioration of symptoms appears so gradually that the surgeon may be tempted (and indeed at times may be forced) to do a thyroidectomy before the patient reaches a euthyroid condition. But if one recognizes beforehand a lengthened duration of preparatory treatment then uses an adequate dose of the drug and exerts some patience and surgical restraint it will be found that practically all patients will ultimately return to normal.

Lahey has called attention to the inadvisability of forcing the patient into a myxedematous state because of the increase in postoperative edema and the possibility of tracheal obstruction. It has been recommended that the drug be discontinued 10 days before operation because of the fear that an agranulocytosis might occur at the time of operation or be induced by the operation. The danger of this complication must be exceedingly small, so small perhaps that it might be disregarded.

Concomitant use of Iodine: Originally thiouracil was administered without iodine but it was soon found that in the diffusely hyperplastic thyroid, friability of the gland made the operation—technically—very difficult. An untreated toxic diffuse goiter is normally friable and vascular; iodine medication reduces the friability and facilitates removal. Thiouracil treated glands seems to be even more friable and vascular than toxic untreated ones. Because of experimental and clinical observations which indicated that the rate of improvement was slowed by previous or concomitant use of iodine, it was recommended that iodine be administered for only the immediate 10 days preceding the operation in order to reduce the degree of friability and in addition prevent the possibility of a crisis.

Further observations indicated that it is better to give the iodine and propylthiouracil simultaneously throughout the period of treatment.[4-13] There is immediate improvement as a result of the iodine followed by the latent effect of the antithyroid drug.

Hibbs and McCullagh[13] have reported a 3.07 percent drop in the basal metabolic rate in toxic diffuse goiter from combined use of propylthiouracil and iodine and a 2.95 percent drop with propylthiouracil alone. From a clinical point of view the combined use of the drugs seems more satisfactory and in addition, the prolonged use of iodine more effectively eliminates the excessive friability. In toxic nodular goiter, however, it is not necessary to administer iodine during the entire preoperative period. It is not particularly effective in reducing the severity of the symptoms in toxic nodular goiter and in addition friability is not a technical problem. Thus in toxic nodular goiter it is perhaps best to give iodine only during the two or three weeks immediately preceding the operation.

Which Patients Should be Prepared with Propylthiouracil? It would be difficult to deny that if a drug can safely return a hyperthyriod patient to a euthyroid condition it should be used in the preoperative preparation of every hyperthyroid patient. The question, of course, arises, "Can this be done safely?" There is every reason to believe that it can. In practice, however, many surgeons for economic reasons find it more convenient to prepare the patients who have mild degrees of hyperthyroidism with iodine therapy alone reserving propylthiouracil treatment for only those with severe degrees of hyperthyroidism. Thus one can find in centers where large number of thyroidectomies are performed that the percent of patients prepared with propylthiouracil varies from 10 percent to a 100 percent. The former figure obtains where most of the patients are from out-of-town and the latter figure where the patients live

in the community and are under the care of an internist.

There can be no doubt that all sick patients, all patients in whom a higher mortality is expected, should be painstakingly prepared for operation by propylthiouracil. The definition of what constitutes a "sick patient" will vary enormously. Perhaps it would be better for the occasional operator to consider all hyperthyroid patients as "sick" and permit the more experienced operator to lower his threshold for propylthiouracil therapy as his experience and capabilities indicate. In this way the mortalities of the two individuals will very likely approximate each other.

A higher mortality can be expected in old patients. In Table I the mortality rate is calculated by decades in 1092 thyroidectomies for toxic goiter. It is seen that though the total mortality is 1.3 percent there was only one death in 511 patients under 40 years of age. Judging from these figures, and they are comparable to the experience of others, it would not be unreasonable to insist that all patients at least over 50 years of age, should be prepared with propylthiouracil.

Preoperative Regime: The vast majority can be treated as office patients. Congestive heart failure and crises are practically the only indications for hospitalization. Before treatment is instituted a basal metabolic rate, a leukocyte count, and perhaps a differential blood count are made. The patient is advised to eat three good meals a day plus additional feedings in the middle of the morning, the afternoon and the evening. Smoking is prohibited before meals. Physical activities are restricted as the general strength of the patient indicates. He must be in bed early, preferably by nine o'clock.

Propylthiouracil is administered, 300 mg. daily, as two 50 mg. tablets three times a day. If the patient has a toxic diffuse goiter he is given five or 10 drops of Lugol's solution in milk or grapejuice three times a day. He is advised to cease taking the propylthiouracil on the appearance of any sort of illness such as sore throat, fever, skin eruption, gastrointestinal symptoms or generalized pruritus and immediately communicate with the doctor. Each week a leukocyte count is made and if it drops to 5000 per cm. a differential count is made. If there is a diminution in the percent of polymorphonuclear leukocytes the propylthiouracil is discontinued.

At each weekly visit the weight, blood pressure and the pulse rate are accurately recorded. From these figures plus the objective observations of general strength and the degree of nervousness and the subjective sensation of the patient it is not difficult to estimate when the patient is euthyroid. A final basal metabolic rate confirms it. The propylthiouracil may be discontinued a few days before operation but the iodine is continued. If the patient has a toxic nodular goiter iodine is given only during the last two weeks of preparation. If auricular fibrillation is present or if the patient is over 60 years of age—mild digitalization is helpful.

Immediate Preoperative Orders: It is well to order a full supper the evening before operation. The food in the gastrointestinal tract does not interfere with a neck operation and the patient needs the extra nourishment. A small amount of one of the phenobarbiturates such as seconal (100 mg. —1½ grains) before bedtime will assure a good night's rest. A similar amount two hours before the operation, morphine sulphate (10 mg. —⅙ grain) and atropine sulphate (0.5 mg. —$\frac{1}{150}$ grain) 45 minutes before operation will give adequate preoperative sedation if inhalation anesthesia is contemplated.

Postoperative Regime: Most patients are more comfortable in a semi-sitting position. Some however acquire a backache from the unaccustomed position and in such a circumstance there is no objection whatever to having the patient lie flat or upon the side. Fluids should be started by mouth as soon as tolerated. Pain, cough or even vomiting are no contraindication.

The administration of intravenous fluids is not mandatory but is advisable. Two thousand cubic centimeters, 1000 cc. of five percent dextrose in physiological saline solution and 1000 cc. of five percent dextrose in distilled water during the first postoperative day is usually adequate. Twenty drops of Lugol's solution placed in the intravenous fluid will supply all iodine requirement for the first day and on the next day the patient may begin with 10 drops three times daily by

mouth. Morphine sulphate (10 mg.—⅙ grain) by hypodermic injection, given freely, will control the pain for the first two days; after that varying doses of codeine and aspirin will suffice.

An oxygen tent is reserved for elderly patients or those who have or have had signs of congestive heart failure. When its use is contemplated it is well to explain the matter to the patient before operation or better still put him in one for a few moments in order to counteract the sense of claustrophobia when he finds himself cooped up in a tent following the operation. If a drain has been placed in the wound it can be removed on the second or third day depending on the amount of drainage or the appearance of the wound.

All sutures or clips must be out in 72 hours. Some patients can get out of bed comfortably and safely on the second day but most of them on the third day. If movement of the neck is encouraged pain and stiffness in the neck, headache and neuralgias are diminished. The average patient leaves the hospital in five, six or seven days. It is imperative that the wound be dressed at least every other day after the patient leaves the hospital.

During the second week, serum frequently collects beneath the scar; it may appear as a small blister or as a soft spot felt along the scar. If one blade of a sharp pointed scissors is inserted in the area a few drops of serous or serosanginuous fluid will exude. If such a collection of serum is not opened, it may extend along the scar spreading apart the edges of the skin. More unsightly scars result from a failure to recognize and puncture these accumulations than result from poor approximation of the skin edges. If the patient had a toxic diffuse goiter the Lugol's solution, five drops twice daily, should be continued for a number of weeks or as long as there are residual symptoms of hyperthyroidism. If the patient had a toxic nodular goiter the iodine is of little value.

Postoperative Complications—"Crisis" or Severe Postoperative Reaction: The term "crisis" or "storm" was used in the past to describe a violent reaction appearing suddenly, usually within 24 hours, and characterized by hyperpyrexia, marked tachycardia, excessive nervousness, delirium and frequently death. Such a reaction is uncommon since the introduction of iodine in the preoperative treatment. The height of the reaction is reached on the second night. The temperature and pulse rate invariably rise on the first evening following operation, drop the following morning, and rise to the highest level on the second night. If, for instance, the temperature is 101° and the pulse rate 110 per minute on the first night they can be estimated at 102° and 130 respectively on the second night. If the temperature rises to 103° the first night, one can expect an additional rise and a troublesome reaction during the second night and thus forewarned, can take anticipatory measures to combat it.

The treatment of a severe postoperative reaction is essentially the same as the routine postoperative treatment, namely, fluids, food, iodine and morphine. Cool sponges, baths, and ice bags help to bring down the temperature. An oxygen tent is usually indicated. Digitalis helps to diminish the deficit in auricular fibrillation. More important is adequate nursing service with special nurses. The inevitable severe reactions occurring in the past should now be exceedingly rare and indeed should be looked upon as prima facie evidence of poor preoperative care or judgment. In elderly people a different type of reaction may occur. In it, the patient without much elevation of pulse rate or temperature, gradually becomes more and more mentally confused, develops mucous and cough, goes into a muttering delirium and dies in a few days with a terminal hyperpyrexia.

Postoperative hemorrhage manifests itself in the following two ways:

1. One of the main vessels breaks loose, the neck suddenly distends, blood pours out through the wound, breathing rapidly becomes impossible and the patient promptly dies unless help is near at hand. The wound should immediately be opened by any means and on the spot. If the carotid is firmly compressed in its midportion, first on one side and then the other, the side from which the bleeding arises can be recognized. Pressure is maintained until additional help arrives and the vessel can be localized.

2. The bleeding is of more gradual origin arising from a small artery or an open vein.

The typical history is about as follows. On the evening of the first day the patient complains that the bandage is tight and that he has much difficulty in swallowing. Fluids "go down the wrong way" and strangle him. The complaints are common enough and little attention may be paid to them unless the blood has oozed to the exterior and saturated the dressings. If the blood collects in the neck without appearing externally, which it not infrequently does, the wound very likely will not be uncovered. As the hours pass a slight inspiratory stridor is heard. If the patient is asked to open his mouth and take a quick deep breath and a noisy inspiration results one can rest assured that trouble is at hand. If nothing is done by the early hours of the morning a loud stridor accompanies each inspiration and breathing is so impaired that cyanosis supervenes. Some of the obstruction is due to direct pressure of the blood clots on the windpipe and some of it to the ever present edema secondary to the pressure. If the surgeon waits too long he may find to his chagrin that when the wound is opened and the clots removed the obstruction is not relieved. When blood collects beneath the deep fascia it causes a diffuse cylindrical swelling of the entire neck. There is edema even up along the borders of the jaw. In most instances it is accompanied by ecchymosis and there is also more than the usual amount of blood upon the dressings. If there is the slightest evidence of tracheal obstruction the patient should be taken to a fully manned operating room and the wound opened without anesthesia. The operation is not an easy one. Frequently the bleeding point cannot be isolated and it will be necessary merely to pack the wound and leave it open.

Obstructive dyspnea has three causes: (1) hemorrhage, (2) recurrent laryngeal paralysis and (3) edema. Collapsed trachea as a cause of obstruction is probably non-existent.[10-11] Hemorrhage has been discussed above. In bilateral recurrent laryngeal paralysis an inspiratory stridor, sometimes barely noticeable and sometimes severe enough to demand a tracheotomy, appears at the time of operation. The vocal cords are in the cadaveric or elliptical position. The voice is hoarse yet the space is large enough for ordinary breathing. However, it is easily obliterated by swelling and edema.

A laryngologist can usually visualize the cords even under the adverse circumstances accompanying a bilateral paralysis, most of us cannot. An excellent method to check the cords is to have the anesthesiologist examine them by direct laryngoscopy after the removal of the first lobe and again after removal of the second lobe. This probably also constitutes the most foolproof method of avoiding a bilateral paralysis. Isolating the nerve as recommended by Lahey[18] is helpful in recognizing the anatomical position of the nerve but is practically impossible in the technically difficult thyroidectomies and does not prevent injury to the nerve cephalad to the inferior thyroid artery.

Edema as the sole cause of obstruction is not common—it is more commonly secondary to a large blood clot. Edema and some obstruction invariably occurs in acromegaly, it is common in myxedema, and is more likely in a man with a short stout neck and in patients with a compressed windpipe. The swelling of the neck is indistinguishable from that produced by bleeding.

In any type of obstruction the patient should be immediately placed in an oxygen tent. On normal inspiration the bronchi are dilated by the negative pressure exerted by the increase in the size of the pleural cavity but there is negative pressure in the tracheal lumen which diminishes its caliber. When there is obstruction there is an increase in inspiratory effort, the negative pressure in the trachea is increased, the cylinder is constricted, the constriction further increases the obstruction. As the effort to breath becomes greater the increasing negative pressure produces an increasing collapse of the laryngeotracheal cylinder until finally, often rather suddenly and unexpectedly, the obstruction is completed and the persistent distal negative pressure maintains it.

If the patient is given oxygen, not only is oxygenation of the lung enhanced but the effort to breathe is lessened and the obstruction is actually relieved. Because of the suddenness of complete obstruction, a tracheotomy set should be in the room and a nurse in constant attendance. In the presence of

hyperthyroidism a tracheotomy is performed early, certainly before recognizable cyanosis. If during an operation postoperative obstruction is considered possible, two silk strings can be inserted into the fascia on each side of the trachea and brought out through the neck untied. If an emergency tracheotomy becomes necessary it can easily be performed by opening the neck, pulling upon the two silk sutures and using them as guide open the windpipe between them. The sutures are harmless and if no obstruction develops they are easily removed.

Parathyroid Tetany: The first symptom of parathyroid deficiency is numbness and tingling in the hands. If the facial nerve is tapped in front of the lobe of the ear, the corner of the lip will twitch. If a blood pressure apparatus on the arm is blown up to above the diastolic pressure, the hand goes into a carpal spasm, but neither of these signs are any more accurate nor do they occur as early as the parasthesia. Furthermore, the numbness and tingling is the last symptom to disappear and it can be used to determine the adequacy of treatment.

Calcium is administered as soon as the symptoms are recognized. If they are mild, two to four grams of calcium lactate by mouth four to six times daily will control them. The amount is reduced as the symptoms diminish but some calcium will be needed indefinitely or at least periodically during the remainder of the patient's life. If the symptoms are severe, calcium gluconate is given intravenously, in addition to the calcium by mouth. If control is not completed by these means, parathormone is indicated. The hormone is effective at the onset but the body sooner or later develops an immunity to it and the substance becomes valueless. Only later and in severe cases of tetany is it necessary to use large amounts of vitamin D or dihydrotachysterol.

Cough and Mucous: There are no criteria by which one can predict the amount of coughing or mucous which will follow a thyroidectomy. It is always present when blood clots collect beneath the deep fascia. It is more common when the operative procedure is more extensive, when the goiter is intrathoracic or the windpipe compressed, or in a thick heavy neck. It certainly is not lessened by intratracheal anesthesia. It is even difficult to correlate the amount of mucuous to the degree of trauma and exposure of the trachea. The symptom can at times become very serious. A weak old lady troubled with mucous may cough until completely exhausted, the mucous collects in the tracheobronchial tree, pneumonia appears and trouble is at hand.

Steam inhalations are definitely beneficial providing the patient actually inhales the steam. Cough mixtures are of no avail unless they contain sufficient codeine to allay the cough. It must be remembered that mucous even in the tracheobronchial tree obeys the laws of gravity. If the patient lies first on one side and then the other its exit is expedited; drainage is further enhanced by the prone position or if worse comes to worse the patient can be held temporarily upside down in an inverted position.

Auricular fibrillation is exceedingly common in elderly people. Its occurrence postoperatively is usually temporary and causes little concern. Treatment consists of relatively small amounts of a digitalis derivative given intramuscularly. The drug is used merely to reduce the pulse deficit and for this purpose not a great deal is required, an ampule of digifolin repeated in four hours and another on the following day will usually suffice.

If the patient continues to fibrillate a week following the operation, Ernstene[12] recommends quinidine sulphate therapy as follows: on the first day two doses of 0.2 grams three hours apart as a test for sensitivity; on the second day three doses of 0.6 grams at two hour intervals; on the third day four doses of 0.6 grams and, if necessary, five doses on the fourth day. This is the maximum dose. Hurxthal[14] rarely uses over 0.4 grams twice daily. He has reported two deaths due to its use.

Deaths: Of the 14 deaths in Table I, nine died of thyrotoxicosis, one of hemorrhage, two of hemiplegia due to embolus, one of mitral stenosis plus hyperthyroidism and one on the table. The following reports of the specific causes of death have been reviewed: Bartlett[6]—1111 operations with 29 deaths, Kroger and Toland[17]—2070 cases with 25 deaths, Bertelsen et al[7]—910 operations with seven deaths, Cole[10]—472 operations with six deaths, Boyce[8]

—952 operations with 38 deaths, McQuillan and Breedenbach[24]—1000 operations with 20 deaths, Young[30]—2933 operations with 54 deaths, Seed—1092 operations with 14 deaths.

These were collected from surgeons especially interested in goiters, from charity hospitals in which mortalities are much higher, from one or more entire hospitals, or an entire community. The above 8756 operations for thyrotoxicosis total 193 deaths—a mortality of 2.2 percent. This probably represents a fair general average of mortality throughout the country.

TABLE 1

OPERATIVE DEATH RATE IN TOXIC GOITER BY DECADES

Age	Number Cases	Number Deaths	Percent Deaths
10-19	49	0	
20-29	187	1	0.2
30-39	275	0	
40-49	291	4	1.3
50-59	190	4	2.1
60-69	90	3	3.3
70	10	2	20.0
	1092	14	1.3

The stated causes of death can be gathered into three groups:

1. "Medical deaths"—deaths due to thyrotoxicosis or to heart failure presumably the result of thyrotoxicosis—97; pneumonia—15; total 112.

2. Deaths presumably due to technical or anesthetic errors—obstructive dyspnea—18; hemorrhage—7; shock—4; on the operating table—6; tetany—1; sepsis—1; total 37.

3. Miscellaneous—emboli—21; more or less unrelated cardiac disease—15; abortion—1; drug reactions—4; gas gangrene—1; infectious hepatitis—1; pancreatitis—1; total 44.

The first group of so-called "medical" deaths—constituting 59 percent of all deaths, at present are in a large measure avoidable. The second group of "technical" deaths, 19 percent, are also avoidable, much the more so now in that speed of operation is less important for recovery and more time and more care can be exerted during the procedure. Of the third group of miscellaneous deaths, 22 percent of the total, embolism probably due to mural thrombi secondary to auricular fibrillation leads the list with heart failure a close second. These deaths are largely unavoidable. Under ideal care the mortality, then, for thyroidectomy for toxic goiter should be about one death in 200 operations. It can be seen that the greatest reduction in the death rate can be accomplished by proper preoperative preparation and a lesser reduction by greater attention to the details of the operation itself.

SUMMARY

Most patients with thyrotoxicosis should be prepared for operation with propylthiouracil. The initial dose is 300 mg. daily. In toxic diffuse or exophthalmic goiter iodine is given concomitantly; in toxic nodular goiter only during the last two weeks of preparation. The white blood count is checked at weekly intervals. Treatment is continued until the basal metabolic rate is normal or nearly normal. The propylthiouracil is discontinued a few days before operation.

The routine postoperative treatment consists essentially of administering iodine, maintaining an adequate fluid and food intake, and controlling pain. Postoperative hemorrhage may occur as a collection of blood in the neck without external bleeding and be evidenced principally by difficulty in breathing. Obstructive dyspnea is due to (1) hemorrhage, (2) recurrent laryngeal paralysis, (3) edema. If the patient is hyperthyroid at the time of operation it must be relieved early.

The other complications peculiar to a thyroidectomy, namely, crises, parathyroid tetany, auricular fibrillation, cough and mucous, are discussed. About three-fifths of the postoperative deaths are due to the thyrotoxicosis in itself. Technical errors account for about one-fifth, a miscellaneous and largely unavoidable group accounts for the remaining fifth. With adequate preparation by propylthiouracil a normal patient can be delivered to the operating room and the operative procedure can be performed with more care and less speed. If this is done most of the causes of death can be eliminated leaving an unavoidable death rate of perhaps one-half of one percent.

RIASSUNTO

La maggioranza dei pazienti affetti da tireotossicosi dovrebbe essere sottoposta ad una cura preoperatoria con propiltiouracile, iniziandola con una dose giornaliera di 300 mg. Negli strumi tossici diffusi e nei gozzi esoftalmici l'iodio va somministrato contemporaneamente al tiouracile: negli strumi tossici nodulari solamente nelle due settimane precedenti l'operazione. Il conteggio dei globuli bianchi va fatto ogni settimana. La somministrazione di tiouracile va continuata fino a che il ricambio basale diventa normale o quasi: va sospesa pochi giorni prima dell'-operazione. Dopo l'intervento, la somministrazione di liquidi e di cibi va mantenuta adeguata: i dolori vanno controllati: l'iodio somministrato. Un'emorragia postoperatoria puo' insorgere, provocando uno stravaso di sangue nel collo, con difficolta' alla respirazione. Dispnea da ostruzione e' dovuta essenzialmente ad (1) emorragia (2) paralisi ricorrente della laringe (3) edema.

L'A. discute altre complicazioni comuni alla tiroidectomia, e cioe'; crisi tireotossiche, tetania paratiroidea, fibrillazione auricolare, tosse. Nei 3/5 dei casi l'esito letale e' attribuibile alla stessa tireotossicosi. Errori tecnici contribuiscono no ad un altro quinto: nel rimanente dei casi la morte e' dovuta a cause varie, spesso inevitabili. Con un'adeguata preparazione con tiouracile i pazienti raggiungono la sala operatoria in condizioni normali, di modo che l'operazione puo' essere eseguita con minore fretta e quindi con maggiore accuratezza. La mortalita' operatoria ha gia' subito una notevole diminuzione: potra' essere ancora ridotta al 0,05%.

SUMARIO

La gran mayoria de los casos de tirotoxicosis se debe de preparar por la administracion previa de la propiltiouracila. La dosis inicial es de 300 mgms al dia. En los casos con exoftalmo o de glandulas de hiperplasia difusa y toxica se administra conjuntamente el yodo.

En los casos toxicos nodulares el yodo se usa en las ultimas dos semanas del periodo pre-operatorio. El tratamiento pre-operatorio se continua hasta que el metabolismo es normal. El propiltiouracil se suspende por unos cuantos dias antes de la operacion.

El tratamiento post-operatorio consiste de la administracion del yodo, nutricion adecuada y el control del dolor. La hemorragia post-operatoria puede ocurrir como una coleccion de sangre en la region del cuello, sin evidencia de hemorragia externa y con dispnea.

La disnea por obstruccion se debe a (1) hemorragia, (2) la paralisis del nervio laringeo inferior, (3) el edema. Esta disnea se debe de corregir lo mas pronto posible especialmente si el paciente fue operado enurante el estado de toxicosis.

Tambien se han discutido las otras complicaciones de la tiroidectomia, tal como las crisis toxicas, el tetano paratiroideo, la fibrilacion auricular, la toz etc. Casi dos tercios de los pacientes que sucumben la causa principal es la tirotoxicosis. Errores de tecnica operatoria son responsable por un 20% de las fatalidades. Con la preparacion adecuada por la propiltiouracil, el paciente esta en condiciones casi normales y por lotanto permite al cirujano el tomar mas tiempo en la operacion evitando asi los errores tecnicos que resultan del apuro. Cuando se eliminan todas estas causa la mortalidad vaja a menos de 0.5%.

SOMMAIRE

La plurat des malades souffrant de thyrotoxicose sont préparés pour l'opération par l'emploi du propylthiouracile. La dose journaliére initiale est de 300 mg. Dans le goître exophtalmique et dans le goître toxique diffus, l'iode est employé en méme temps. Dans le cas de goître nodulaire toxique, on l'emploi seulement dans les deux semaines qui précèdent l'opération. A intervalles hebdomadaires, le compte des globules blancs sanguins est observé. Le traitement est continué jusqu'a ce qu'on ait obtenu un métabolisme basal normal ou presque normal. On discontinue le propylthiouracile quelques jours avant l'opération. Le traitement postopératoire habituel consiste essentiellement de l'administration de l'iode, du maintien adéquat de fluide et du contrôle de la douleur. L'hémorragie postopératoire peut survenir comme collection de sang dans le cou sans hémorragie externe

et se manifeste principalement par une respiration difficile.

La dyspnée obstructive est dûe:

1. À hémorragie.
2. À la paralysie du nerf laryngéal.
3. À l'édéme.

Si le malade est hyperthyroïdique au temps de l'opération, la dyspnée doit être soulagée sans délai.

Les autres complications qui peuvent survenir aprés la thyroïdectomie, sont: crises, tétanieparathyroïdiennes, toux et production excessive de mucus, et sont discuteés. A peu près 3/5ème des cas de décès postopératoires sont dûs a la thyrotoxicose même. Des erreurs techniques sont responsables pour le 1/5ème et un groupe de conditions divers inévitables représente l'autre 1/5ème.

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General Surgery

The Surgical Management of Chronic Ulcerative Colitis*

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AS ONE reviews the available literature pertaining to the management of chronic ulcerative colitis, much confusion becomes manifest in that no definite procedure is universally applicable for all cases. Because of this flexibility the rationale of its management—medical or surgical—continues to remain a moot question.

The treatment of chronic ulcerative colitis is essentially a medical problem, yet it is conceded that for patients who do not respond to a precise medical regime and for those who develop complications, surgical intervention is definitely indicated. Streicher [1] has calculated that 20 percent of patients suffering with this disease will be cured by medical management; 60 percent will show improvement with periods of exacerbation and remission, and 20 percent will result in total failure. Surgery ceases to be considered the last desperate effort to prevent fatal disaster. However, it is recognized as a means of preserving life in the presence of acute sepsis and to rehabilitate those in a state of chronic invalidism. As Kiefer and Jordan [2] have stated, "the medical treatment of chronic, idiopathic ulcerative colitis must be regarded as a control and not a cure—complete colectomy is the only actual cure of chronic ulcerative colitis now available." While we do not hold with this statement in its entirety, it is conceded that the results acclaimed from a strictly medical regime are most discouraging.

The most widely used surgical procedure is ileostomy, performed either as a palliative maneuver or as a preliminary step to resection. Appendicostomy and cecostomy have their proponents as well, although in our experience, both are inferior to ileostomy since, in so many instances, the cecum and distal ileum are involved.

Transversostomy may be well chosen in those cases where the disease is confined to the left colon and rectum. The indications for ileostomy may be enumerated as follows: sepsis not amenable to rigid medical regime, remissions and exacerbations of the disease, uncontrollable diarrhea, impending perforation and chronic malnutrition or anemia. Jordan and Bargen both postulate that ileostomy should be reserved for the complications and those intractable cases where at least two or three flare-ups of the disease have already been dealt with medically without appreciable benefit. We cannot concur with the opinion of Marachella that surgical intervention admits defeat and should be postponed until all trial and error methods have been exhausted, which leaves the patient in a deplorable physical state in the vast majority of instances.

Ileostomy as an emergency procedure carries with it a high mortality, 53 percent in the series reported by Cave,[3] and 75 percent reported by Cattell.[4] Such can readily be appreciated because these patients are usually too ill to withstand any type of surgery. Peritonitis should not be considered an indication for ileostomy. Whether or not hemorrhage warrants ileostomy is open to question since we all have experienced at least one instance where failure has occurred. Ileostomy as an elective procedure offers a low mortality (6 to 9 percent).[3,4] It is to be emphasized that the disease should never be permitted to progress beyond a point where, in the opinion of both the surgeon and the internist, the patient becomes a poor surgical risk. An ileostomy may be established as either a temporary or permanent procedure. Large groups of cases are not available from which one may deduce

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whether subsequent closure can be satisfactorily effected. According to the few reported at hand, approximately two thirds can be so treated. Crohn [5] never advises closure once it is made, but considers it an initial step to resection.

One must be ever mindful of the complications associated with ileostomy among which may be mentioned: retraction, contraction or prolapse of the stoma, obstruction, perforation, volvulus, abscess and fistulae in the abdominal wall around the stoma; repeated collapse from sudden salt deprivation as a result of abrupt and profuse diarrhea, skin irritation, urinary complications and anemia.

Vagotomy which has been employed in the treatment of duodenal ulcer has been performed by Dennis [6] in cases of this disease. Based on the demonstration that postganglionic sympathectomy in dogs was followed by lesions suggesting clinical colitis in man, and on the marked relief of gastrointestinal spasm following division of the vagi for duodenal ulcer, this investigator recently reported his experiences with vagotomy in twenty two cases of idiopathic ulcerative colitis and in one case of functional diarrhea. Gastrointestinal studies following vagotomy revealed marked slowing in gastric emptying. Prolongation of intestinal transit, even when gastric emptying began immediately, was shown. Dennis mentions that the best clinical results followed vagotomy in cases of short duration or with mild demonstrable fibrosis.

Colectomy has been popularized during the past few years and, while the procedure is a formidable one, it is surprising to observe how well patients tolerate extensive resection with present day management. Patients for whom an ileostomy has been established and who present signs and symptoms of persistent sepsis, extensive scarring of the bowel, fibrous stricture, pseudopolypoid and malignant degeneration, as well as arthritic change, should be colectomized. The operation may be performed as a single stage or multiple stage procedure. Ordinarily, an ileostomy is made as the initial step and, following a varying period of time, the right, transverse, and left colon are removed. Thereafter, the rectum and lower sigmoid are excised by an abdominoperineal maneuver.

While complete colectomy is usually indicated, there are many instances where partial colectomy or segmental resection can be satisfactorily performed. Ileosigmoidostomy and ileorectostomy are frequently recommended either as a delibrate therapeutic approach, or as a preliminary to colectomy. To this, the authors cannot subscribe since the percentage of patients who are free and remain free of disease in the rectum and sigmoid are extremely few.

It is recognized that this disease begins in the rectum and sigmoid in more than 90 percent of all cases. This is confirmed by Bargen and others. In Jordan's series of 430 patients with chronic ulcerative colitis, the rectum was involved in 407 or 94 percent. It is, therefore, our frank opinion that the rectum should be extirpated except in the very exceptional case.

Some mention should be made pertinent to transplantation of an ileostomy to the anus with sphincter preservation following colectomy. Rudolph Nissen,[7, 8] formerly of Istanbul, reported such a procedure in 1933 for multiple polyposis. Ravitch recorded his experiments on dogs in 1947,[9] and this year cited his experience with ingenious modifications in five patients with chronic ulcerative colitis.[10] Ravitch states that neither incontinence nor excoriation of the anal skin has been a problem and that complete sphincter continence and good sphincter tone are gradually regained after operation. Wangensteen did employ this method in two instances but because of skin excoriation was compelled to replace the ileum to the abdomen. Babcock similarly performed this procedure in three instances of ulcerative colitis and for the same reason returned the ileal stoma to the abdomen in two. Payne and Hay each had one case in which replacement to the abdomen was necessitated by marked degree of excoriation.

In the presence of impending perforation, ileostomy may be well chosen. On the other hand, in peritonitis, it is probably better to employ "watchful waiting" with antibiotic and chemotherapeutic measures. Obstruction calls for surgical decompression, while stricture, pseudopolyposis and malignant degeneration demand colectomy.

Anorectal abscesses occurring during the

course of the disease require incision and drainage, but correction of other pathology, such as hemorrhoids should ordinarily be treated conservatively.

Our experience has been particularly limited. Of the ileostomies performed, either as an emergency or elective procedure, the mortality rate has been 21 percent.

There were, however, twelve colectomies, either total or partial, without death; with the exception of one, the rectum had been removed. The following tabulation shows the cases reported by various surgeons:

Author	Cases of Ileostomy	Mortality	Cases of Ileosigmoidostomy	Cases of Colectomy	Mortality
Cave	65	18.0%	11	55	10.9%
Cattell	83	14.5%	—	54	20.0%
Garlock	15	13.3%	6	16	18.7%
Garlock	38	15.7%	21	46	10.8%
Bargen & Pemberton	130	26.9%	20	30	36.3%
McKittrick	54	27.7%	—	10	10.0%
Lemmer	17	23.5%	4	11	18.0%
Rankin	26	31.7%	—	—	—
Ferguson	14	?	—	9	14.2%
Best	8	12.5%	—	—	—
Ault	—	—	—	13	15.3%
Wangensteen	—	—	—	13	none
Bacon	19	21.0%	—	14	none

SUMMARY

Customarily all of our patients are placed on a rigid medical regime which briefly includes individualized diet, adequate vitamins, transfusions of blood and plasma with regular frequency and in small amounts, parenteral administration of protein derivatives, and sulfathalidine alternating with neoprontosil. At no time have we ever hesitated to employ anti-amebicides such as emetine, even though repeated mucosal scrapings and stool specimens are negative for the parasite. Where severe exacerbations and remissions of the disease have occurred on two or three occasions, surgical intervention is indicated. Ordinarily, a preliminary ileostomy is established and subsequent colectomy, provided the case conforms to its indications as previously outlined. Removal of the rectum, in our experience, has been required as the final step.

RIASSUNTO

I pazienti vengono ordinariamente sottoposti ad un regime medico rigoroso, il quale include: una dieta selezionata; la somministrazione di una quantita' adeguata di vitamine; piccole, ripetute trasfusioni di sangue e di plasma; somministrazione parenterale di derivati di proteine; sulfaptalidina alternata con neoprontosil. Anche allorquando l'esame batteriologico e' riuscito negativo, antiamebici sono stati frequentemente usati. La cura medica e' stata sostituita dalla cura chirurgica allorquando la colite si e' esacerbata per due o tre volte. Quando indicata, una colectomia e' stata eseguita dopo un'ileostomia preliminare. L'escisione del retto e' generalmente richiesta quale ultima tappa operatoria.

SUMARIO

Generalmente nuestros pacientes son sometidos a un regimen medico estricto que consiste de una dieta individualizada, rica en vitaminas, de transfuciones de sangre o de plasma en pequenas cantidades y que se repiten con regular frecuencia; infuciones intravenosas de derivados proteicos, y la administracion oral de la sulfatalidina alternandose con la neo-prontosila. En casos dudosos se usan los amebicidas, tal como la emetina, aunque el examen repetido del excremento sea negativo. En casos de recurrencia seria la intervencion quirurjica es indicada. Ordinaria-

mente se hace una ileostomia preliminar y despues se practica la colectomia, siempre y cuando esta sea indicada. En nuestra experiencia la reseccion del recto es un paso final.

SOMMAIRE

Nous mettons nos malades sous un régime sévère qui comprend une diète individualisée; des vitamines en quantité adéquate, des transfusions de sang et de plasma à intervalles réguliers et en petites quantités, de l'administration parentérale de dérivés de protéines, et aussi en ingestions de sulfathalidines alternant avec la néoprontosile. Nous n'avons jamais hésité de nous servir d'anti-amébicides telle que l'émétine, même si le curettage de la muqueuse et les échantillons des fèces ne demontrèrent pas la présence de parasites. En présence de récidives des symptomes et de rémissions, répéties l'intervention chirurgicale est pratiquée.

Ordinairement, nous faisons une iléostomie préliminaire et, si les indications sont conformes, suivie de colectomie. Si l'état du malade l'exige, nous enlevons le rectum. Dans notre expérience, cela fut nécessaire dans plusieurs cas.

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Radical Amputation for Cancer of the Breast With and Without Irradiation

A Statistical Study*

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A GREAT many studies have been reported, relating to the surgical treatment of breast carcinoma, dealing with the work of one surgeon or one clinic. This paper deals with 1212 radical amputations of the breast, performed by many surgeons working in four Minneapolis hospitals.

The records of these hospitals for the past 20 years were used for this statistical report. The four hospitals have a bed capacity of 1475 and yearly admissions of 34,770.

The main considerations in this paper are: the clinical stage of the disease at operation; the five year survivals resulting from surgery, with and without irradiation; and a comparison between the large and small tumors.

The entire report is concerned with the results of treatment and not its technique.

Table 1a and 1b contain some important statistics relating to the patients at the time of operation and also some information concerning the postoperative period. They show that 61.7 percent of the tumors were reported Scirrhus, 8.8 percent Adenocarcinoma, 6.8 percent Medullary and 22 percent Unclassified.

The youngest patient was 17, and the oldest patient was 93, with an average age of 53 years. The highest age incidence was in the fifth and sixth decades.

Of the 89 percent which were married, 65 percent had borne children. The single group totaled 11 percent.

A family history of cancer was obtained in a little over a fourth of the cases, with six percent reporting Trauma and five and one-half percent with previous diseases of the breast.

The average age for beginning menopause was 45 years. Tumor duration at the date of operation, ranged from a very short time to many years, with an average of 13½ months. Pain of different types and degrees was complained of by more than half of the patients.

Five percent of the group had some discharge from the nipple, described as bloody, watery, or containing pus.

The tumors were equally divided between the two breasts—45½ percent were located in the upper, outer quadrants.

Regional metastases were found in more than half of the patients—mostly axillary. Remote metastases appeared postoperatively in 47 percent of the cases in the following locations: spine, pelvis, ribs, liver, brain, ovaries, mediastinum, lungs, pleura, pancreas, rectum, uterus, glands and generalized metastases. A total of 10 percent of the cases had recurrence of the growth in the scar.

The 1212 cases were classified into two clinical stages. Stage one included the group in which the tumor was confined to the breast. This numbered 584 cases. Stage two contained those cases where both the breast and axilla were involved and where there was to a limited extent, adherence of the tumor to the skin, nipple retraction or elevation, or fixation to the underlying muscle. This stage numbered 628 cases.

Table 2 shows the five year survival rates according to stage.

Only those patients operated upon five or more years previous to the date of inquiry—which was January 1, 1948—were eligible. This group numbered 1060. However, only 951 could be traced for five or more years—456 of these being in stage one and 495 in stage two. This tracing was done through letters to the patients themselves, to their relatives, through hospitals, doctors, use of city directories, and through city and state departments of health.

The five year survival rates were figured

* Presented at the Thirteenth Annual Assembly of the United States Chapter of the International College of Surgeons, St. Louis Nov. 15-20, 1948.

TABLE 1a

Total Cases	Classification		Age Incidence		Marital Status		Family History of Cancer	Trauma	Previous Disease of Breast
No.	Types	%	Age Groups	%	% of Married	% of Single	%	%	%
1212	Scirrhus	61.7	17—24 yrs.	.05	89	11	27	6	5.5
	Adeno	8.8	25—29 yrs.	1.34					
	Medullary	6.8	30—39 yrs.	11.8					
	Paget's	.05	40—49 yrs.	26.9					
	Ca Unclass.	22.0	50—59 yrs.	27.4					
			60—69 yrs.	22.2					
			70—79 yrs.	8.7					
			80—93 yrs.	1.3					

Statistical information relating to the 1212 cases in the series.

TABLE 1b

Age at Beginning Menopause	Duration of the Tumor at Operation	Pain was Present	Discharge from the Nipple	Location of the Tumor		Metastases Present		Recurrence in the Scar
				Site	%	% of Regional	% of Remote	%
45 yrs.	13½ Mo.	55	5	Upper outer Quadrant	45.5	51.8	47	10
				Lower outer Quadrant	12			
				Inner upper Quadrant	10			
				Inner lower Quadrant	6.5			
				Central Zone	12			
				Upper half	7			
				Lower half	7			

as the ratio in percent of those patients who lived five or more years after operation, to the number of traced patients in that particular stage.

It was found that 70.3 percent in stage one had survived for five or more years—almost double that of stage two, which was only 38.7 percent. A total of 513 patients survived for five or more years, which was more than half of the 951 traced patients.

Table 3 shows the survival rates according to stage, for five, 10, 15, 20 and more year survivals.

This table shows that 62.6 percent of the stage one, five or more year survivals, actually lived for five to nine years inclusive, and 68.7 percent in stage two lived for the same length of time. This five to nine year group has a much higher percent of five year survivals than any other group. The percent of survivals in each of the groups becomes increasingly less, with increased length of sur-

vival. It is interesting to note that the percent of survivals is higher for the stage one patients —with the exception of the five to nine year group.

Table 4 is a study of the 951 patients, traced and eligible for five year survival, grouped according to the size of the tumor. This was to discover, if possible, whether or not the size affected the survival rates. Patients with tumors of two centimeters or less in diameter, were put into one group and those of more than two centimeters, in another.

Small tumors numbered 250, while 701 were large. In stage one, 77.3 percent of the patients with small tumors attained five year survival and only 63 percent of those with large tumors. This shows that those patients with small tumors, had a 14 percent higher survival rate.

In stage two, only 46 percent of the patients with small tumors, reached five year survival —much less than in stage one. Only 37 percent of those with large tumors in stage two, survived for five years.

This table seems to indicate that patients with small tumors, have a much greater chance for five year survival.

Table 5 groups the five or more year survivals, according to the duration of the tumor at operation and according to the size. This was to see whether a difference in the length of the tumor duration in the small and large

TABLE 2. FIVE YEAR SURVIVAL RATES ACCORDING TO STAGE

	Patients Operated Upon				Lived 5 or more years after Operation	
	Total	Eligible* for Study	Traced* Patients Number	Percent of Traced Patients	Number	Percent of Traced Patients
Stage I	584	518	456	88	321	70.3
Stage II	628	542	495	91.3	192	38.7
Summary	1212	1060	951	89.7	513	53.9

* Inquiry as of January 1, 1948. Included here are only those patients operated on five or more years prior to the date of inquiry, i.e., 1942 or earlier, and only those that were traced.

TABLE 3. FIVE, 10, 15, 20 AND MORE YEAR SURVIVALS—ACCORDING TO STAGE

	Total Patients Operated Upon, who lived 5 or more years after Operation*								
	Number	Lived 5 to 9 yrs. inclusive	%	Lived 10 to 14 yrs. inclusive	%	Lived 15 to 19 yrs. inclusive	%	Lived 20 or more yrs. inclusive	%
Stage I	321	201	62.6	78	24.3	31	9.6	11	3.4
Stage II	192	132	68.7	40	20.8	18	9.3	2	1.0
Summary	513	333	64.9	118	23.0	49	7.5	13	2.5

* Inquiry as of January 1, 1948. Included here are only those patients who were operated upon in 1942 or earlier, who lived for five or more years after operation and who were traced.

TABLE 4. FIVE YEAR SURVIVAL RATES ACCORDING TO THE SIZE OF THE TUMOR

	Eligible and Traced Patients*	Patients with tumors 2 cm or less in diameter, who were eligible for 5 year Survival			Patients with tumors over 2 cm in diameter, who were eligible for 5 year Survival		
		Number	Number of Survivals	Percent of 5 year Survivals	Number	Number of Survivals	Percent of 5 year Survivals
Stage I	456	159	123	77.3	297	198	63
Stage II	495	91	42	46.0	404	150	37
Summary	951*	250	165	66.0	701	348	49.6

* Only 951 of the total 1212 patients operated upon, were eligible and traced for five year survival.

TABLE 5. FIVE YEAR SURVIVAL RATES ACCORDING TO THE DURATION OF THE TUMOR, AND ACCORDING TO THE SIZE

Size of Tumor	Stage	5 Year Survivals	Tumor Duration in 5 Year Survivals							
			1 day to 5 mo., inclusive		6 to 12 mo., inclusive		13 mo. to 2 yrs. inclusive		Over 2 yrs.	
		No.	No.	%	No.	%	No.	%	No.	%
Small Tumors	I & II	144	78	54.1	39	27.0	13	9.0	14	9.7
Large Tumors	I & II	299	138	46.1	83	27.7	36	12.0	42	14.0
Summary	I & II	443*	216	48.7	122	27.5	49	11.0	56	12.6

* Only 443 of the 513, five or more year survivals, reported their tumor duration at operation.

tumors, made any difference in the number of five year survivals.

Only 443 of the 513, five year survivals reported their tumor duration at operation.

The one day to five months group in both the small and large tumors, contained the largest percent of five year survivals. The other duration groups showed a decrease in the percent of survivals, as the length of the tumor duration increased—with the exception of the *over two year group.*

Table 6 is a comparison of five year survival rates of those patients who had irradiation and those who did not. The group of irradiated patients included those who had radium, x-ray or both—preoperatively, operatively, or postoperatively.

More than half of the patients in stage one

TABLE 6. FIVE YEAR SURVIVAL RATES ACCORDING TO STAGE AND IRRADIATION

	Eligible and Traced Patients	Patients who had Irradiation				Eligible and Traced Patients	Patients who did *not* have Irradiation			
				Patients who lived 5 or more years after Operation					Patients who lived 5 or more years after Operation	
	No.	No.	%	No.	%	No.	No.	%	No.	%
Stage I	456	253	55.5	178	70.3	456	203	44.5	143	70.4
Stage II	495	341	68.8	129	37.8	495	154	31.1	63	40.8
Summary	951*	594	62.4	307	51.6	951	357	37.5	206	57.8

* Inquiry as of January 1, 1948. Included here, are the 951 patients who were operated upon five or more years previous to this date, and so were eligible for five years survival study.

TABLE 7. FIVE YEAR SURVIVAL RATES ACCORDING TO STAGE, SIZE OF TUMOR AND IRRADIATION

	Irradiation in 5 Year Survivals						Non-Irradiation in 5 Year Survivals					
	5 Year Survivals		Size of Tumor				5 Year Survivals		Size of Tumor			
	No.	%	Small	%	Large	%	No.	%	Small	%	Large	%
Stage I	178	70.3	59	33.1	119	66.8	143	70.4	64	44.7	79	55.2
Stage II	129	37.8	24	18.6	105	81.3	63	40.8	18	28.5	45	71.4
Summary	307*	51.6	83	27.0	224	73.0	206*	57.7	82	39.8	124	60.1

* See Table 6.

TABLE 8. STATUS OF THE 1212 CASES IN THE SERIES ON JANUARY 1, 1948

	Total Operated Patients	Total Traced Patients 1-1-48	Patients Alive on January 1, 1948				Patients Dead on January 1, 1948			
			Without the Disease	With the Disease	Total Alive 1-1-48	% Alive 1-1-48	Without the Disease	With the Disease	Total Dead 1-1-48	% Dead 1-1-48
	Number	Number	No.	No.	No.		No.	No.	No.	
Stage I	584	523	241	6	247	47.2	63	213	276	52.7
Stage II	628	569	126	2	128	22.5	67	374	441	77.5
Summary	1212	1092	367	8	375	34.3	130	587	717	65.6

—55½ percent—had irradiation, while 44½ percent did not. The result was that 178 of the irradiated patients in stage one, lived for 5 or more years. Their survival rate was 70.3 percent.

The 143 of the stage one non-irradiated patients, also lived for five or more years, with a survival rate of 70.4 percent. So, the survival rates for this stage were practically the same whether the patients had irradiation or not.

For stage two patients, almost the same situation holds for 37.8 percent of the irradiated patients survived for five or more years and 40.8 percent of the non-irradiated.

According to *this* study, irradiation makes very little difference in the survival rate.

Table 7 is a comparison of five year survival rates, to learn whether the size of the tumor—both with and without irradiation—made any difference in the survival rates.

This table shows that a much greater percent of the tumors in the five year survivals —both irradiated and non-irradiated—were large tumors, over two centimeters in diameter; that the small tumors in stage one—both irradiated and non-irradiated—produced higher survival rates than those in stage two; that the large irradiated tumors of both stages, produced higher survival rates than the non-irradiated. This last would seem to prove that irradiation is especially beneficial for large tumors of both stages.

Table 8 shows the present status of the 1212 cases in the series.

On January 1, 1948, 1092 of the 1212 patients were traced. On that date, 47.2 percent of the stage one patients, were alive and 52.7 percent were dead. Of the stage two patients 22½ percent were also alive on that date and 77½ percent were dead.

A total of 717 patients were dead—587 having died of the disease. Of the total dead, 36 percent had lived from five to 22 years postoperatively, with an average of seven and one-half years each. On January 1, 375 patients were living which is more than a third of the total traced patients. Some of them had lived for more than 20 years after surgery.

SUMMARY

1212 radical amputations for breast cancer, performed by many surgeons in four hospitals, are studied from a statistical standpoint.

The cases are divided into two clinical stages at operation, depending upon whether the tumor is confined to the breast, or metastasis has taken place.

The traced patients, eligible for five year survival, numbering 951, are studied to learn the survival rates. This is found to be higher for stage one than for stage two patients.

The cases are grouped to learn whether the duration of the tumor, the size, or irradiation, makes any difference in the survival rates.

The final outcome for the total number of 1092 traced patients, is studied to ascertain how many are alive on January 1, 1948. The percent of the dead who died of the disease is especially noted.

CONCLUSION

When treatment for breast cancer is carried out while the disease is confined to the breast —clinical stage one—better results are obtained than after it has spread beyond the breast—clinical stage two.

Patients with tumors of short duration have a better chance for five or more years survival than those with long duration.

Irradiation does not appreciably increase the number of five year survivals in either clinical stage one or stage two. However, irradiation of large tumor patients of both stages appears to be of great benefit.

Radical amputation for breast carcinoma, with irradiation for the large tumors in both clinical stage one and stage two appears to be the treatment of choice, according to this study.

The age of greatest breast cancer incidence is in the fifth and sixth decades. However, women of all ages should examine their breasts frequently and have their doctor do so every six months. They should be made aware of the fact that breast cancer discovered early and treated early, has the more favorable prognosis.

RIASSUNTO

L'A. afferma ancora una volta che i risultati operatori sono migliori allorquando il tumore e' encora limitato alla mammella e sviluppato da non troppo tempo. La terapia attinica non

eleva apprezzabilmente la percentuale di sopravvivenza dopo i cinque anni. E' utile sopratutto allorquando il tumore e' molto voluminoso. L'A. ritiene che l'asportazione radicale della mammella, con irradiazione complementare nei tumori voluminosi, rappresenti tuttora la cora di elezione. Richiama anch'egli l'attenzione sopra la necessita' che ogni donna (e piu' specialmente quelle nel 5°-6° decennio) si sottoponga ad un controllo periodico, possibilmente ogni sei mesi. Cio' in base ad una prognosi migliore per i cancri scoperti precocemente.

SUMARIO

Cuando se trata el cancer de la mamma, que aun esta confinado a esta glandula– estado clinico #1,– los resultados son mas satisfactorios que cuando esta enfermedad ya ha pasado de los confines de la glandula– estado clinico #2–.

Los pacientes con tumores de poca duracion tienen mas probabilidades de sobre-vivir cinco anos y mas, que aquellos con larga duracion.

La irradiacion no aumenta apreciablemente la sobre-vivencia de cinco anos o mas en los casos en el estado clinico #1 o en el #2. Sin embargo la irradiacion en casos de tumores grandes en ambos estados clinicos aparentemente es de gran beneficio. La amputacion radical de la mamma, con irradiacion de los tumores grandes en ambos estados clinicos, parece ser el tratamiento de seleccion, de acuerdo con este estudio.

El cancer de la mamma es mas comun en la quinta y sexta decadas de la vida. Sin embargo toda mujer no obstante su edad debe de examinar sus pechos frecuentemente y tambien por su medico cada seis meses. Ellas debe de ser educadas a la realizacion que el cancer en sus comienzos tiene un prognostico mas favorable.

SOMMAIRE

Dana le cancer du sein, tant que la maladie est confinée au sein, on obtient de meilleurs résultats que lorsque le cancer s'est étendu au-delà du sein. La malade présentant une tumeur récente a une meilleu chance de survivre cinq ans ou plus, que quand la tumeur est de longue dâte; l'irradiation n'augmente pas d'une façon notable la survivance de cinq ans; néanmoins l'irradiation des grandes tumeurs parait être d'une certaine utilité. L'amputation radicale d'une tumeur du sein, suivie d'irradiation, est le traitement du choix. L'incidence des cancer du sein est plus grande durant la cinquième et sixième décades de vie. Néanmoins, la femme de tout âge devrait examiner fréquemment ses seins et consulter son docteur régulièrement. C'est un fait reconnu que la cancer du sein diagnostiqué et traité en temps voulu fournit un pronostic plus favorable.

Extra Abdominal Rerouting of the Bile Flow in Irreparable Bile Duct Destruction

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THE final results of plastic reconstruction of the common biliary duct are not encouraging. Recurrent obstruction is the rule, rather than the exception. There are three causes of failure.

1. Cicatricial stenosis at the anastomosis of bile duct and intestines.

2. Accumulation of sand or concrements within the remaining or newly constructed bile passages.

3. If inorganic tubes are used then their passage into the intestinal canal is, as a rule, in a short time followed by obliteration of the area where the tube was anchored. Vitallium tubes, which were very much in favor at one time, may even become acutely dangerous since they are apt to create pressure necrosis.

In cases where every attempt of plastic repair has ended in failure, a satisfactory result can be expected only by a method which permits, at frequent intervals, dilatation and mechanical cleansing of the new connection between hepatic duct and intestinal tract. The simplest solution of this problem would appear to be an extra-abdominal passageway for the bile. *This can be done by creating an external biliary fistula which, is connected by means of a rubber tube to an excluded loop of jejunum, transplanted into the adjacent subcutaneous tissue.* The only objection to such a procedure is that, in the absence of a sphincter mechanism, the intestinal contents can be forced in to the biliary duct system causing ascending biliary infection, however, experiences with short-circuiting cholecystojejunostomy, choledochoduodenostomy and hepatico duodenostomy have shown that this disadvantage has little practical significance.

We have been unable to find definited unequivocal values of biliary pressure in man under pathological conditions. Nevertheless it was felt that in a patient with a prolonged history of biliary stasis, recurrent progressive obstruction and repeated ascending cholangitis, structural and functional changes may have taken place in the liver parenchyma and the intrahepatic duct system which would enable it to produce bile under abnormally increased pressure and thus overcome the pressure of the intestinal contents.

On the basis of these theoretical considerations and in view of the fact that all other conventional means of internal anastomosis between the biliary passages and the intestinal tract had already failed, this above-mentioned simple kind of external rerouting of bile flow was instituted in a patient whose history reveals the following important facts.

CASE HISTORY

Female, age 40; April 1944, cholecystectomy for cholelithiasis. The surgeon described the operation as uneventful and typical. In the first days following operation, there was increasing jaundice, large collection of bile in subphrenic and subhepatic space. Both collections were drained through the previous abdominal incision. As drainage of the subphrenic space was insufficient, a transdiaphragmatic incision of the subphrenic space was performed four weeks after the original cholecystectomy.

Injection of lipiodol into the remaining biliary fistula gave evidence of a rather long stenosis of the common and the hepatic duct.

Revision—June 22, 1944: Only the peripheral end of the common duct was found to be intact, but very narrow. No bile was obtained from this end of the common duct. The entire hilus of the liver was occupied by dense scar tissue. The idea of end-to-end anastomosis of the common and hepatic duct was abandoned. The external biliary fistula was followed into the hepatic duct and a hepatico-duodenostomy performed over a rubber tube. There was temporary improvement; stools regained normal color.

Seven weeks later, readmission to the hospital with coliky pains, high temperature. Preoperative diagnosis: recurrent bile duct

obstruction. Relaparotomy. The rubber tube was removed; it was filled with concrements and sand. Central to the tube retention of turbid white bile and pus was found. A large rubber tube was again inserted into the hepatic duct and a hepatico-gastrostomy performed over this tube. Symptoms of cholangitis subsided within ten days postoperatively.

Six weeks later again obstructive symptoms (jaundice, temperature). X-ray picture showed that the tube had passed into the stomach. Relaparotomy. The tube was extracted from the stomach. The former canal of the tube was filled with stones and sand. A Goetze type of hepatico-jejunostomy was performed. Uneventful recovery.

Patient was comfortable for about a year. Then again chills, fever, jaundice, vomiting and coliky pains. Relaparotomy June 5, 1946. Exposure of anastomosis revealed stenosis by constricting heavy scar tissue; retention of infected bile, concrements, and sand central to the anastomosis. In view of the repeated reformation of concrements, it was felt that any kind of anastomosis would again become defunctionalized, by sand and sediment of bile concrement. Therefore, a F24 catheter was inserted into the hepatic duct for about 10 cm. and brought out through the abdominal incision after epiploic omentum had been wrapped around the tube. The excluded jejunal loop, which at the previous operation was used for the hepatico-jejunostomy was then exposed and another tube inserted into this jejunal loop by a Witzel type of jejunostomy, and brought out of the abdominal wall about 6 cm. medial to the point of exit of the hepatic tube.

The hepatic tube was permitted to drain bile into a bottle for a few days and after adequate drainage was observed, it was connected with the jejunostomy. After about two weeks, when it was felt that adequate canalization of both the hepatic and jejunal fistula had occurred, these tubes were removed and replaced by a F24 whistle tip catheter which was introduced at the end for about 10 cms. into the hepatic duct and at the other directly into the jejunostomy. The patient had an uneventful recovery with her temperatures gradually reaching normal values, her jaundice subsiding and her stools becoming brown in color.

The patient has since then lived for two years and three months and during this time, her condition has—with some remissions—steadily improved. The main difficulty during the first six months was management of the two fistulae which put the patient's as well as her husband's endurance to a great test. Three months postoperatively she was hospitalized for three days in order to irrigate and cleanse the hepatic fistula which had become obstructed with debris. About four months later, she developed cholangitis and was admitted to the hospital for nine days, receiving streptomycin 200,000 units every three hours for one week. Her temperature was normal during this time and her pain subsided.

During the following year, the patient's general condition gradually improved. Her weight increased from 92 to 100 pounds. The pain and discomfort on the right side became less frequent and less intense in character. However, it was necessary for her to be treated regularly in order to keep the biliary fistula in working condition. Granulating tissue at the external orifice had to be cauterized to prevent blockage of the canal and the tube had to be changed from time to time. There was also a certain amount of skin irritation around both orifices and we found after some experimentation that aluminum powder was the most effectual means of keeping the skin protected and clean. Occasionally the biliary fistula had to be dilated but all these procedures became necessary with less frequency during the course of the following 15 months. At the end of this time, after the patient had failed to report for a check-up for four and a half months, she developed a stenosis of the external orifice of the biliary fistula and was hospitalized for five days. The biliary fistula was enlarged by bilateral splitting of the skin surrounding the external opening which had contracted. The inside tract was dilated with Hegar dilators up to F24, after which a good flow of bile was obtained. A new F24 catheter was placed into the biliary fistula and the jejunostomy. Patient was discharged in excellent condition with normal temperature.

Since that time, she has led a fairly normal life attending to her usual domestic duties. She had learned how to take care of catheter and how to keep the skin around the fistulous openings clean. The only dressing

required was a small piece of 4 x 4 gauze and a strip of elastoplast to hold it in place. She complained of little pain, had normal temperatures and gradually gained in appetite and weight. She was even able to go swimming without ill effects. Unfortunately, about one-half year later, the patient sustained a fatal head injury in an accident and died from a subdural hemorrhage.

We feel, however, that a two year-three month survival period with gradual improvement in general health would indicate the feasibility of the above described method in cases of complete destruction of the hepatic and common bile duct where other methods of internal anastomosis have failed.

SUMMARY

In a patient where repeated attempts of reconstruction of the extrahepatic bile ways ended in failure because of formation of concrements, an extra abdominal passageway was instituted. Thus mechanical cleaning of the bile way in regular intervals became possible.

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The Acute Surgical Abdomen*

PHILIP THOREK, M.D., F.A.C.S., F.I.C.S.
CHICAGO, ILL.

A SURGEON, no matter how seasoned or skilled, will always be confronted with the annoying perplexities presented to him by the acute abdomen. After examining the charts from the surgical services at the Cook County Hospital for a period of ten years, I have found six outstanding conditions which we mistake most frequently. They are:

1. Perforated peptic ulcer.
2. Acute appendicitis.
3. Acute cholecystitis.
4. Renal colics.
5. Acute hemorrhagic pancreatitis.
6. Coronary occlusion.

Although coronary occlusion is not a surgical emergency, its correct diagnosis becomes of surgical importance when exploration is considered. There is a seventh disease which deserves special consideration, namely, salpingitis. Acute or chronic salpingeal pathology is frequently associated with a perihepatitis which produces pain in the right upper quadrant (pseudo-gallbladder pain). Because of this, gallbladder explorations and other surgical procedures have been done in cases of salpingitis, resulting in danger to the patient and embarrassment to the surgeon.

PERFORATED PEPTIC ULCER

Although not first in frequency among the conditions mentioned, the perforated peptic ulcer holds a place of primary importance in the diagnostic difficulties which it presents. This condition is rare in females. Usually a previous history of peptic ulcer or hemorrhage can be obtained, but the onset may be with perforation.

The patient states that he was seized with a sudden pain, usually after eating; this was so severe that it doubled him up. The classical picture of perforated peptic ulcer with board-like rigidity and a shock-like syndrome is too well known to bear repetition. Two signs which should be sought for in every case, however, are: (1) the findings with auscultation, and (2) the presence of pneumoperitoneum. Auscultation reveals an absolutely silent abdomen when an ulcer perforates, leaks and soils the peritoneal cavity. This is not new, since the late J. B. Murphy had stressed the importance of this finding many decades ago. When intestinal sounds are present, the diagnosis of perforated peptic ulcer is remote. There are exceptions, and one of these will be discussed presently under the subject of forme fruste ulcer.

The next sign which helps clinch the diagnosis is the demonstration of a spontaneous pneumoperitoneum. Normally a magenblase or stomach air bubble is present. When an ulcer perforates, this air bubble escapes into the general peritoneal cavity, and can be demonstrated either by percussion or with the fluoroscope; the latter is by far the more accurate. The patient is placed on his left side so that the free air bubble may gravitate upward between the liver and the right hemidiaphragm. By so doing, the liver is displaced downward and is separated from the diaphragm. Normally the liver hugs the diaphragm and no air space is visible between them. If this air is of an appreciable amount, normal liver dullness is obliterated and in its place a tympanitic note is produced by percussion. The sign is easy to demonstrate, quite pathognomonic of perforated peptic ulcer, and present in about seventy percent of all cases.

The forme fruste ulcer deserves special mention. The term refers to a pin-point perforation in the stomach or duodenum which is immediately sealed over by muscular contraction or by the overlying liver. Therefore, the spillage is minimal and the amount of peritoneal soiling is small. Such patients may experience a sudden sharp pain in the epigastrium, but the typical physical findings are lacking. This patient may be able to straighte

* Presented at the Thirteenth Annual Assembly of the United States Chapter of the International College of Surgeons, St. Louis, Mo., Nov. 15-20, 1948.
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up and walk about. Abdominal sounds are usually present and the air bubble may remain intragastric, having had no chance to leave the small perforation. These patients present a misleading picture and have been misdiagnosed. However, with the ingestion of their next meal they usually reperforate and then present the typical findings.

The temperature, pulse and respirations will depend upon whether or not shock is present. Most perforated peptic ulcers present a shock-like picture which varies in its intensity. The shock associated with perforated ulcers responds rapidly to therapy. Within a few hours, the classical picture of peritonitis develops with the associated increase in temperature, pulse and respiratory rate.

The contents from a perforated ulcer may pass downward along the so-called "paracolic gutter of Moynihan," pool around the appendix and produce exquisite tenderness at McBurney's point. The diagnostician must then be on his guard, since such a history would suggest an epigastric distress with localization to the right lower quadrant which could be confused with an acute appendix. Upon exploratory operation, free fluid will be found in the peritoneal cavity with all signs of a peritonitis, and a red and injected appendix seen and removed. These patients usually die if the leaking ulcer is overlooked. This catastrophe can be avoided if, before closing the abdomen, the appendix is opened and the mucous membrane examined. Since acute appendicitis starts in the lumen of the appendix and travels outward, a normal appearing mucous membrane would suggest looking elsewhere for the cause of the peritonitis.

Laboratory data includes the flat x-ray film which has been discussed under the subject of spontaneous pneumoperitoneum. Routine blood count and urinalysis are done. Some of these patients might have bled, and although perforated ulcers are known not to produce massive hemorrhage, signs of a secondary anemia may be present.

ACUTE APPENDICITIS

The more one sees of this condition the more one respects it. The statement "only an appendix" is indeed a dangerous one. Acute appendicitis is most frequently found in individuals under the age of forty and is somewhat more common in males. It will be recalled that gallbladder conditions appear most frequently after the age of forty. The story that the patient relates is usually quite stereotyped. To put it in his language: "Something I ate gave me a bellyache." This is his way of describing acute epigastric distress. When he gets this "bellyache" he often attempts to obtain relief with either a cathartic or an enema. Within the first twenty-four hours his "bellyache" becomes a soreness low on the right side. His acute epigastric distress has become localized to the right lower quadrant.

The "two-question test" is both useful and time-saving. *Question Number One:* "Where was your pain when it started?"; to this interrogation the patient points to his entire abdomen. *Question Number Two:* "Where does it hurt you now?"; he then points to the right lower quadrant, usually McBurney's point. This simple method of having the patient demonstrate diffuse pain which localizes to the right lower quadrant will diagnose the vast majority of cases of acute appendicitis.

Vomiting and nausea have been impressed upon us as being associated with appendicitis. This is the exception and not the rule. Anorexia, or loss of appetite, is more constant and more important than either nausea or vomiting. Anorexia, nausea and vomiting are three degrees of one symptom; anorexia is the mildest form and is associated with mild distention of the appendix; nausea, the middle degree, is due to moderate distention; and vomiting, the maximum degree, is found in greatly distended appendices. The most common symptom in acute appendicitis is anorexia, and if the patient states that his appetite is not altered we doubt the diagnosis of an acute appendix. Two complaints which are extremely rare in acute appendicitis are diarrhea and chills. These are probably found in less than one percent of the cases. Constipation is the rule.

Fever is not an early finding in acute appendicitis; in fact, if present, it is suggestive of peritoneal soiling. It is true that cases of acute appendicitis may have a fever of 102° or 103°, but these are no longer cases of appendicitis; they are cases of far advanced

peritonitis. Children prove the exception to this rule. If appendices would be operated upon when the temperature is below 99° the mortality would be very low.

Acute appendicitis does *not* give right rectus rigidity. Although the reverse is taught in many schools and textbooks, this point should be clarified. It is impossible for an individual to contract his right rectus muscle without contracting the left, therefore, when pressure is made upon an inflamed area, both rectus muscles contract. When only one rectus is rigid it suggests an underlying mass, such as a tumor or abscess. When both recti contract to pressure it should be considered "muscular defense" rather than right or left rectus rigidity. The importance of this bears emphasis when we realize that diagnosis, treatment and prognosis may depend upon the presence of right rectus rigidity or simple muscular defense.

The iliopsoas and obturator signs are not signs which diagnose actue appendicitis, but rather locate an acute appendix. Probably a misconception has arisen because these signs are usually discussed under the heading of acute appendicitis; they may, however, be produced in other diseases. The right iliopsoas sign is elicited by placing the patient on his left side and hyper-extending the right leg. If positive, pain is produced over the iliopsoas fascia which will be manifested in the region of the right lower quadrant. In the presence of a history of acute appendicitis this would signify that the inflamed appendix is overlying the iliopsoas fascia and is retrocecal. A positive obturator sign will locate an inflamed pelvic appendix. It is conducted in the following way: with the patient on his back the thigh is flexed upon the abdomen and the leg upon the thigh; the leg is then abducted. This causes internal rotation of the thigh and stretches the obturator internus muscle. If this produces pain it is diagnostic of a fasciitis involving the obturator fascia, which could be caused by an inflamed tube, appendix, ovarian cyst, etc. If the patient elicits a history of acute appendicitis with a positive obturator sign, we conclude that the appendix is low-lying and in the pelvis. Rovsing's sign is also helpful. It is elicited by pressing over the left cecum; the colonic gas which has been pushed to the right will produce pain over the cecal region, which is quite diagnostic of acute appendicitis.

Routine bi-digital examinations are done; at times an acute appendix or appendiceal mass may be felt. Late and neglected appendices may produce a pelvic abscess which points rectally or vaginally, and this examination reveals the proper site and time for incision and drainage.

The laboratory data usually consists of a white blood count and a urinalysis. More important than the white blood count or urinalysis is a differential blood count; this is easy to do and more accurate. If the "poly" count is high, we assume that an acute infectious process is present; a high "poly" count in the presence of a low white count means a poor prognosis. The urinalysis is usually negative but may be misleading; a few red cells in the urine are not pathognomonic of renal pathology. Negative urines have been recorded where a renal stone completely blocks the ureter so that no blood or pus can pass into the bladder.

Flat x-ray films are of value in the diagnosis of acute appendicitis. If an opaque stone casts a shadow on the right side, one readily realizes that this may be located either in the appendix, the ureter, or gallbladder; phleboliths must also be considered. Stereoscopic views, intravenous pyelography, and the nature of the opaque shadow cast will usually locate the region in which the stone is located. If such a stone appears to be in the appendix, this almost always is diagnosed as an acute appendicitis.

ACUTE CHOLECYSTITIS

The dictum that certain types of people are predisposed to certain types of diseases seems to be correct. The gallbladder type is described as being fair, fat and forty, usually a female in the latter third or fourth decade and somewhat obese. There is always an exception to the rule, hence, the most fulminating hydrops of the gallbladder on our service was seen in a young thin boy of sixteen. The age of forty is related to a previous history of pregnancy, and this is theoretically explained in the following way: the average female has her children in the second decade of life, and

while pregnant she develops a physiologic hypercholesterolemia. Some of this cholesterol deposits on the mucous membrane of the gallbladder, forms polypi which break off and become the nuclei for stones. It may take from 10 to 20 years for gallstones to attain any appreciable size, so that by the time she reaches her fourth decade the stone is large enough to obstruct or irritate. Nulliparous women can also have gallstones or gallbladder disease, but this too is the exception and not the rule.

In the middle aged female the history of recurrent attacks of abdominal pain, so severe that the physician must administer a sedative, is an acute gallbladder until proved otherwise. Acute appendicitis does not require morphine; renal colics will be differentiated presently, and coronary occlusion is rare in the female. One of the most unusual lesions noted in the female is a perforated peptic ulcer. The gallbladder patient also presents a previous history of "selective dyspepsia." By this we mean that there are certain specific foods that she cannot tolerate. There are four primary offenders to these foods, they are: fried and fatty foods, raw apples, cucumbers and cabbage. The patient does not use the term "dyspepsia," but describes this distress as the two "B's," namely, bloating and belching. To summarize and describe the gallbladder patient one may use an alliteration and state that she is the patient with the seven "F's": she is the fair, fat, fertile, flatulent, flabby, female of forty.

The complaint is one of pain, and it is important to determine the type of pain which is present. A constant pain is due to edema, but colicky pain is caused by obstruction. This is one of the factors which indicate whether the case be treated conservatively or surgically. It is unwise to treat an obstructed lesion conservatively, since these are cases which result in early gangrene and perforation. Morphine should not be used in gallbladder disease because it is a smooth muscle contractor, and since the gallbladder is a smooth muscle organ one should not administer a medicament which would stimulate its activity. By increasing muscle tonus, morphine may actually aggravate or provoke gallbladder pain and colic.

One should not state, however, that the drug must never be used in gallbladder disease, since it still has its place, namely, to prevent shock. These patients are treated first with nitrite therapy. One breaks an amyl nitrite bead and lets the patient inhale the vapors; 1/100th grain of nitroglycerin is placed under the tongue, and three grains of sodium amytal or any other barbiturate is given by mouth. If this gives no relief we administer a hypodermic which consists of 100 mg. of demerol and 1/100th of a grain of nitroglycerin. Should these measures fail, antispasmodic therapy with such drugs as papaverine, aminophylline, et cetera, is tried. Morphine is used only after all other measures have failed.

Gallbladder pain is usually located under the right costal margin, but may be referred to the stomach since these two organs originate from the same embryologic segment. The stomach responds to this stimulus in one of three types of gastric spasm: (1) pylorospasm, (2) midgastric spasm and (3) cardiospasm. If a pylorospasm is produced, the gallbladder condition might be confused with peptic ulcer; if midgastric spasm results, a stomach carcinoma may be erroneously diagnosed; and if associated with cardiospasm, the pain appears on the left (pseudo-coronary pain), and coronary disease may incorrectly project itself into the diagnostic picture.

Radiation of pain should not be confused with referred pain. By radiation we mean that gallbladder pain, located under the right costal margin, may radiate along the path of the seventh intercostal nerve to the inferior angle of the right scapula, or the interscapular region. Gallbladder pain, therefore, cannot radiate to the right shoulder. Shoulder pain is an entirely different mechanism which involves the phrenic nerve and is indicative of peritonitis. When a gallbladder patient has true shoulder pain a diagnosis of gangrenous or ruptured gallbladder with biliary peritonitis should be made.

Temperature, pulse and respirations are included under the heading of physical examination. The patient with an acute gallbladder has an early high fever, hence, a temperature of 102° is not unusual within the first 12 to 24 hours of acute cholecystitis. The early fever is explained by the absence of a submucosa. Since this tough resisting layer

is lacking, there is greater chance for early contamination and absorption in the peritoneal cavity. The patient has a pulse which is increased according to the temperature; therefore, for every degree rise in fever there will be approximately a ten beat increase in pulse rate. Respirations are slightly increased because breathing is painful. This is due to the fact that the inflamed gallbladder rubs against the sensitive parietal peritoneum; because of this, acute gallbladder disease may be confused with pneumonia or pleurisy.

Although pain, a symptom, may be referred anywhere along its nervous path, tenderness, a physical finding remains at the site of pathology. This is an excellent diagnostic rule, having few if any exceptions. The tenderness of gallbladder disease will be located in the region of the right costal margin. If it is most marked on a level with the umbilicus, it may be difficult to determine whether the condition is an inflamed, low-lying gallbladder or an acute high-lying retrocecal appendix.

Two ways aid in the differentiation of these two conditions. First, we recall that the normal abdomen reveals a tympanitic note to percussion in all four quadrants. If the tenderness opposite the umbilicus is due to an inflamed gallbladder, we assume that the organ is unusually large or that a ptotic liver with an inflamed gallbladder at its free border is present. This would cause an obliteration of the normal tympany in the right upper quadrant and in its place the percussion note would be one of dullness or flatness. If the patient presents tenderness on the level with the umbilicus and retains normal tympany in the right upper quadrant, this would point to a high-lying retrocecal appendix.

Another method of differentiating the gallbladder and appendix is by means of Ligat's test. This test locates areas of hyperesthesia over an inflamed organ. If the tenderness is due to gallbladder disease an area of hyperesthesia (elicited by picking up the skin and letting it drop) is present from the umbilicus upward to the right costal margin. If the tenderness is due to an acute appendix, the area of hyperesthesia will be found from the umbilicus down to Poupart's ligament.

A rectal examination is done as a routine in every physical examination. More important than the rectal or vaginal examination is a so-called bi-digital, which is conducted by placing the index finger in the vagina and the middle finger in the rectum with the perineum in between. This will immediately orient the examiner and adnexal pathology will be revealed.

A flat x-ray film should be taken in every acute abdominal condition. One may determine whether a calcified gallbladder or visible stones are present. It also gives an indication as to whether or not the liver is enlarged or ptotic. Routine laboratory tests are done.

RENAL COLICS

Stones are not the only substance which produce renal colics, since the same syndrome may be produced by a small blood clot, inspissated pus, uratic debris, or a kinking of the ureteropelvic junction in a ptotic kidney.

The condition is more common in males, and the patient may reveal a history of previous attacks, a hereditary influence, a story of gout, or parathyroid pathology.

The patient complains of a sudden pain which starts in the lumbar region and radiates to the testicle, vulva, or the inner aspect of the thigh. With this pain he becomes extremely restless and thrashes about. A patient who is experiencing a colic is restless and moves about, but one who has a peritonitis lies perfectly quiet and resents being moved. Vomiting is a common symptom as is a frequency of urination. During the act of micturition the pain may be altered.

Physical examination rarely reveals any elevation in temperature, but extremely characteristic of the condition is a bradycardia. It has ofttimes been stated that when a patient with an acute abdomen has "a clean tongue and a slow pulse" he has a renal colic until proved otherwise. Tenderness is most marked in the region of the twelfth rib of the involved side, and to elicit this finding it is unnecessary and cruel to utilize any type of "punch" test. The tenderness is so exquisite that mild percussion will demonstrate it. We prefer to use the term "Murphy tap" to "Murphy punch." A zone of hyperesthesia is usually found posteriorly at the level of and slightly below the twelfth rib. If this area

is anesthetized with novocaine, the hyperesthesia and pain disappear.

A flat x-ray film may reveal a stone if such is present, but this is not reliable since nonopaque substances may also produce kidney colic. An intravenous pyelogram can be made without disturbing the patient, and if necessary the film can be taken at the bedside with the aid of a stationary grid. The significant finding for a diagnosis of a stone in the ureter is the anuria which may be present on the affected side; the opposite side shows normal excretion. The kidney on the affected side usually appears increased in density since the dye in these tubules is more concentrated. This finding is sufficient for diagnosis of nonopaque stones in the ureter. A catheterized specimen of urine usually reveals pus, blood and albumin. The presence or absence of pus and blood in the urine is not pathognomonic since a stone may completely block the ureter and result in a normal urine. On the other hand, an inflamed appendix may be attached to the ureter, kidney or bladder, resulting in a secondary ureteritis, nephritis or cystitis with an associated hematuria. In such instances the laboratory report may be actually misleading.

ACUTE HEMORRHAGIC PANCREATITIS

It is important to recall that this disease may appear in one of two forms: either acute edematous pancreatitis or hemorrhagic pancreatitis. The former presents a mild clinical picture, but the latter which is associated with fat necrosis and occasionally a hemorrhagic peritonitis produces a fulminating one. The acute edematous form usually improves rapidly without therapy within 48 hours, but hemorrhagic pancreatitis gets progressively worse and often requires surgical intervention. It is the hemorrhagic type, therefore, which is important to identify and treat promptly.

Although the etiology of pancreatitis is unknown, there seems to be a mechanical factor which is associated with spasms, stones, swelling and stasis. The patient who develops acute pancreatitis is usually of the same type who develops gallbladder disease, therefore, the condition is more common in females, rarely occurring before the age of forty, and is seen in stout people. The ratio of colored to white is 1 to 50. The attack usually follows the ingestion of a heavy meal. The pain is dramatic, sudden and excruciating. It is felt in the epigastrium, and radiates into one or both loins. In this way pancreatic pain radiation resembles an inverted fan. When the patient sits up or lies on his abdomen, the pain is relieved, and is aggravated when he is on his back. Hence, in most pancreatic conditions, be they tumors or inflammations, the patient is usually found lying on his abdomen or in a sitting position. Reflex vomiting or retching almost always occurs; emesis which is truly reflex in nature is never feculent.

Physical examination reveals a patient who is usually in shock with cold and clammy extremities, subnormal temperature, and a rapid, thready pulse. Local epigastric tenderness is almost always present and is associated with a type of muscular defense which is localized to the same area. The rigidity is not truly board-like in nature, and the tenderness is most marked midway between the umbilicus and the xiphoid. An occasional finding is ecchymosis in one or both loins, or at times around the umbilicus. This is due to extravasated blood which finds its way around the retroperitoneal space and presents itself as greenish yellow or purplish discolorations. This finding takes two or three days to appear. Mild jaundice is present in about half of the cases; this is explained by the fact that the common duct is pressed upon by a swollen head of the pancreas. Abdominal auscultation usually reveals a quiet but not silent abdomen.

Laboratory findings may be helpful in the diagnosis. An increase of serum amylase is specific in the acute phase, although a normal reading does not rule out acute pancreatitis. Polowe has emphasized the importance of determining the blood amylase activity in terms of cuprous oxide precipitation. He has shown that moderate to marked blood amylase activity is almost always associated with diseases of the pancreas, and normal or decreased blood amylase almost always excludes pancreatitis. Hypocalcemia is usually present and the level found is usually below nine. A flat x-ray film of the abdomen may reveal a separation of the upper and lower limbs of the duodenum

brought about by an edema of the head of the pancreas. This latter finding is unusual.

CORONARY OCCLUSION

Although this belongs to the realm of the internist, the general practitioner as well as the surgeon must be on his guard to avoid the fatal error of confusing an acute coronary disease with an acute abdominal condition.

Men are most susceptible to this condition, and it is usually found in those past the age of forty. A previous history of dyspnea or pain in the chest during exertion or excitement may be elicited. The attack is sudden, with severe pain in the chest which radiates out the left arm toward the abdomen or both shoulders. There is a sense of impending death with severe fright which usually supersedes the complaint of pain. The radiation may also be toward the epigastrium, so that the examiner's attention is directed to the abdomen rather than the chest. A usual complaint during such an attack is one of "indigestion." Although the pain of acute coronary disease may occur in the abdomen, it does not become localized, hence, no area of local tenderness is ever found. Marked abdominal distention may be present in coronary pathology but muscle or rectus rigidity are lacking.

In abdominal catastrophes the patient lies perfectly quiet, but the coronary patient resembles the colic in that he is restless and tosses about. The acute cardiac patient presents veins in the neck which are distended and full, in contrast to the patient with the surgical abdomen who may appear pale and bloodless. Signs of impaired circulation are usually present, such as dyspnea, orthopnea and cyanosis. Auscultation will usually reveal rales in both bases due to pulmonary congestion. Cardiac enlargement, feeble heart sounds and occasionally a pericardial friction rub may be found. During auscultation of the abdomen, normal intestinal sounds will be heard which are absent or diminished in cases of peritonitis.

Positive electrocardiographic findings are pathognomonic, but one is not always fortunate enough to have an electrocardiogram handy. A leukocytosis may be present some hours after the disease takes place, and the urine is usually negative unless there is associated renal pathology.

We realize that many other conditions at times require differentiation in the acute abdomen. Some of these are: strangulated herniae, regional ileitis, mesenteric lymphadenitis, mesenteric thrombosis, ruptured ectopic pregnancy, ruptured graafian follicle, ileocecal tuberculosis, vasitis, torsion of the omentum, volvulus, intussusception, etc., etc., ad infinitum. However, when one misses one of these unusual conditions he does not feel quite as responsible or guilty as he would having missed one of the aforementioned "Big Six."

SUMMARY

Perforated peptic ulcer, acute appendicitis, acute cholecystitis, renal colics, acute hemorrhagic pancreatitis, and coronary occlusion, are the six outstanding conditions which the author states are most frequently misdiagnosed in cases of the acute surgical abdomen. Although coronary occlusion is not a surgical emergency, its correct diagnosis becomes of surgical importance when exploration is considered. A seventh disease is also named which is, salpingitis. Acute or chronic salpingeal pathology is frequently associated with a perihepatitis which produces pain in the right upper quadrant (pseudo-gallbladder pain). Because of this, gallbladder explorations and other surgical procedures have been done in cases of salpingitis, resulting in danger to the patient and embarrassment to the surgeon.

After a thorough probing of the six aforementioned conditions, the author reports that many other conditions at times require differentiation in the acute abdomen. Some of these are: strangulated hernia, regional ileitis, mesenteric lymphadenitis, mesenteric thrombosis, ruptured ectopic pregnancy, ruptured graafian follicle, ileocecal tuberculosis, vasitis, torsion of the omentum, volvulus, intussusception. However, misdiagnosing one of these unusual conditions is more explanable than missing the symptoms of the *primary six.*

RIASSUNTO

Le malattie che conducono piu' frequentemente ad un attacco acuto sono: ulceri peptiche perforate, appendicite acuta, colecistite acuta, colica renale, pancreatite emor-

agica acuta, occlusione delle arterie coronarie. Quest'ultima condizione, per quanto non di pertinenza chirurgica, puo' coinvolgere un problema chirurgico allorquando venga posto in considerazione un intervento operativo.

Una salpingite acuta o cronica, spesso associata ad una periepatite, con dolori nel quadrante superiore destro, puo' rientrare nella diagmosi differenziale, perche' molte operazioni inutili, che danneggiano la paziente ed imbarazzano il chirurgo, sono state eseguite in casi dubbi.

Dopo aver discusso le caratteristiche cliniche di queste diverse condizioni morbose, l'A. no elenca molte altre, meno comuni, che richiedono volta per volta una diagnosi differenziale nell'addome acuto. Fra le tante: ernia strangolata; ileite regionale; linfadenite mesenterica; trombosi mesenterica; gravidanza ectopica; rottura di follicoli di Graaf; tubercolosi ileo-cecale; torsione dell'omento; volvolo; intuscezione. Un errore nella diagnosi differenziale e' piu' facilmente spiegabile che l'ignorare i sintomi delle diverse malattie.

SUMARIO

En la experiencia del autor, la ulcera peptica perforada, la apendicitis aguda, la colecistitis aguda, el colico renal, la pancratitis hemorragica aguda, y la oclusion de la arteria coronaria, son las seis condiciones que se confunden mas frecuentemente en el diagnostico del abdomen quirurgico agudo. El reconocimiento de la oclusion de la coronaria es de importancia en el diagnostico diferencial de las emergencias quirurjicas. La salpingitis es la septima enfermedad que tambien debe de considerarse. La salpingitis aguda o cronica esta frecuentemente asociada con la peri-epatitis que produce dolor en el quadrante supraumbilical derecho (dolor pseudo-vejical). Por esta razon exploraciones de la vejiga de la hiel se han practicado erroneamente en casos de salpingitis, con peligro del paciente y resultante embarradura del cirujano. El cirujano por lo tanta debe de proceder con cuidado en el diagnostico diferencial de las condiciones mencionadas y en ciertos casos debe de tambien considerar las condiciones siguientes: La hernia estrangulada, la enteritis regional, la linfadenitis mesenterica, la trombosis del mesenterio, el embarazo ectopico, la ruptura del foliculo de Graf, la tuberculosis ileo-cecal, torcion del omento, el volvulo, la intusucepsion intestinal, Sin embargo el errar en el diagnostico de estas enfermedades es mas excusable por cuanto no son comunes, no asi las seis primeras mencionadas.

SOMMAIRE

L'ulcère peptique perforé, l'appendicite aigüe, la cholecystite aigüe, les coliques rénales, la pancréatite hémorragique aigüe et l'occlusion coronaire, sont les six conditions qui sont le plus fréquement diagnostiquées faussement dans les cas de l'abdomen chirurgical aigü. Quoique l'occlusion coronaire ne soit pas une lésion chirurgicale urgente, son diagnostic est d'une grande importance chirurgicale, quand on discute la nécessité d'intervenir opérativement. Il faut aussi considérer la salpingite. La pathologie aigüe ou chronique des trompes de Fallope est fréquemment accompagnée d'une périhépatite produisant des douleurs dans le cadran supérieur droit. A cause de ceci, l'exploration de la vésicule biliaire et d'autres procédures chirurgicales ont été faites, dans des cas de salpingite; il en ait résulté du péril pour l'opéré et de l'embarras pour l'opérateur. Apres avoir discuté les six conditions ci-dessus mentionnées, l'auteur nous dit qu'il y a d'autres conditions qui doivent être différenciées dans l'abdomen aigü. Parmi celles-ci, on peut énumerer: l'hernie etran glée, l'iléite régionale, la lymphanédite mésentrique, la thrombose mésentrique, la rupture des grosses ses ectopiques, la rupture des follicules graafiens, la tuberculose iléocécale, la torsion de l'omentum, le volvulus et l'intussuception. Il est plus excusable de se tromper dans ces conditions que dans les six conditions citées au debut de cette communication.

Congenital Valves of the Posterior Urethra

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CONGENITAL valves of the posterior urethra are frequently the causative factors of a series of urinary complaints which invariably and inevitably result fatally unless surgical intervention is instituted. The great variance of symptoms portrayed and the intensity of the symptoms frequently make differentiation from other infravesical obstructive factors impossible, except by complete urologic examination. Too frequently, a diagnosis of "chronic pyelitis" or more often a diagnosis of eneuresis is offered without the benefit of urological examination. A complete urological examination should always be considered in every instance of continued pyuria or eneuresis in either sex. Anomalies of the genito-urinary tract are among the most common malformations observed in the human body. Granted that although a percentage of these anomalies is not manifested either by primary or secondary symptoms until later in life, the majority of instances are observed within the first few months or years after birth. The presence of pyuria and infection are secondary symptoms which result from stasis of urinary flow. It is now an established fact that stasis of the urinary flow, regardless of the position of obstruction, predisposes to urinary tract infection. It becomes obvious that any child presenting protracted or recurrent pyuria should have the benefit of complete urological study to ascertain the presence or absence of obstructive factors.

Until recent years, the diagnosis of congenital valves of the posterior urethra was recognized only at postmortem or by accident during an operation for some other condition. The knowledge of the obstructive factors of congenital valves is well-established and it is not believed that the number of reported cases is at all a fair estimate of the frequency with which the condition actually occurs. It is firmly believed that the condition is not so rare as the sparsity of reported cases in the literature would suggest. As frequently as congenital valves of the posterior urethra have been observed during the past few years it is quite obvious that even today, the condition occurs more often than is recognized. Campbell considers that the anomaly known as congenital valves of the posterior urethra is the second most common of all congenital infravesical obstruction. As recently as 1937 he was able to collect only a total of 166 references in the literature. Since that time there are 38 additional references bringing the total to 204 cases. To this number, three cases herein reported are to be added.

Case 1. L. W. 18 months old white male, admitted to Temple University Hospital on the Pediatric Service with a history of failure to gain weight in nine months. a tendency to respiratory infection, marked constipation, and a large abdomen. Patient was well for six months after birth. At that time he had an attack of vomiting, cyanosis and constipation. At 13 months of age he developed acute diarrhea with low grade fever, malaise and anorexia. These symptoms persisted for five days but recurred after one month.

On admission, the abdomen was prominent and large fecal masses were palpable. After numerous enemas, a suprapubic mass, smooth and firm extending to the umbilicus was palpable. Barium enema revealed no evidence of organic disease of the colon and showed the suprapubic mass to be anterior and separate from the colon. Cystographic study revealed "considerable distortion of the urinary bladder. There is a spherical cyst-like compartment superimposed upon the major portion of the bladder. The upper margin of the dye filled bladder is approximately at the level of the umbilicus. A considerable amount of the opaque material passed up the left ureter which is visualized as an unusually large and tortuous structure and the kidney pelves did not visualize."

Intravenous urography was done. The examination was continued for three hours and at no time was there any evidence of the appearance of dye on either side of the upper urinary tract.

Cystoscopy was performed. "The cystoscope was introduced into the bladder at an extreme angle. The bladder is dilated. The mucosa is extremely pale and markedly trabeculated. The vesical orifice is markedly contracted and irregular. The inter-

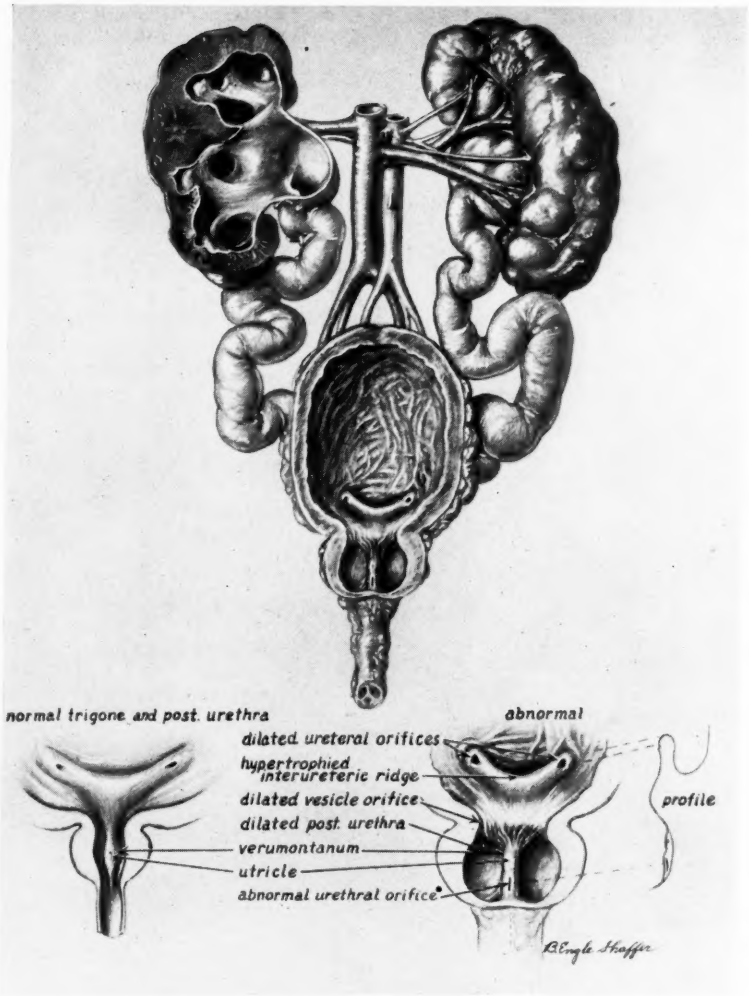

Fig. 1. Artist drawing of genito-urinary tract as observed at autopsy. Note the greatly dilated ureters and kidney pelvis and calices. Note lower right insert showing the abnormal urethral orifice located on the verumontanum and the greatly dilated posterior urethra. Also note the marked trabeculations, the hypertrophied interureteric ridge, and the dilated ureteral orifices. It is considered that modification of type 3 is demonstrated.

ureteric ridge is markedly hypertrophied and gives the appearance of two bladder cavities."

Following cystoscopy, the temperature rose to 104.6 and continued for 48 hours in a typical septic fashion. On the morning of the third day, a distinct mass developed and was palpable in the left loin. The mass was considered to be a hydronephrosis. In view of the septic temperature and the presence of a mass in the loin, a decision was made to institute immediate nephrostomy drainage. The patient expired from acute cardiac dilatation during the surgical procedure. An autopsy was granted and performed. The report of the pathologist is as follows:

"The genito-urinary tract is removed in toto. Both kidneys appear enlarged. Protruding from the left pelvis is a rubber catheter. There is uniform dilatation of both ureters. Each capsule strips easily, revealing a pale grayish pink smooth cortical surface. Upon sectioning, one finds the distention of the pelves and calyces has caused pressure atrophy of the renal parenchyma. In some places the cortico-medullary layer is only 1.5 cms. thick. Cloudy fluid fills the pelves. The pelvic lining is hyperemic and granular. No source of obstruction is encountered in the ureters. The ureteral walls are thin and the mucosa is flattened. There is considerable distention of the bladder with increased volume capacity. The wall is thin and the mucosal lining trabeculated. No obstruction is found at the ureteral orifices. There is a marked interureteric ridge."

The urethral opening is widely opened and a diffuse dilatation of the prostatic urethra has resulted in the formation of large cyst-like structure surrounded by a thin layer of prostatic tissue. A probe inserted at the urethral meatus easily passes through the penile urethra, however the latter is not continuous with the prostatic segment and the probe instead emerges from a tiny slit in the verumontanum approximately 2 mms. in size. This small opening being entirely inadequate readily explains the urinary retention and the obstructive sequillae (Fig. 1).

In retrospect. The abdominal mass extending to the umbilicus was a greatly dilated bladder and not a cyst of the urachus as was surmised. On cystoscopy, what was considered to be the hypertrophied interureteral ridge was in reality the greatly dilated vesical orifice. What was considered to be the contracted vesical orifice was the edges of the sinus in the verumontanum through which the cystoscope entered the greatly dilated posterior urethra.

Case 2. W. A., 19 year old colored youth was admitted to Temple University Hospital on the Medical Service in a semi-comatose condition having suddenly become drowsy. Examination on admittance showed an unresponsive hyperemic individual lying flat in bed. Blood pressure was 130/90. Polyuria was present, the urine having a fixed specific gravity at 1007. Blood urea nitrogen was 100 mgms. Following treatment improvement occurred to a point of being able to walk around. He gave a history of having been examined in another institution six years previously. A diagnosis of congenital strieture of the urethra and of the ureteral orifice and a bilateral hydronephrosis was made. He did not return for treatment.

Subsequent study showed that the blood urea nitrogen remained at 100 mgms. An intravenous urogram showed no concentration of dye. A cystogram revealed a dilated bladder and dilated ureters as well as massive distention of both calyceal systems.

Cystoscopy revealed a marked congestion of the entire versical mucosa. Extensive bullous edema involving the entire trigone and obliterating the ureteral orifices was noted. The vesical orifice was widely dilated as was the posterior urethra. Rectal examination revealed a very highly situated prostate and a distinct firm transverse ridge extending across the rectum above the prostate.

An attempt was made to institute decompression by indwelling Foley catheter. He was unable to tolerate the catheter. Approximately one week before death, the blood pressure rose to 190/120. The patient developed an enlarged liver as well as marked dysponea. Acute congestive failure was so severe that he expired.

Autopsy was granted and performed. Examination of the genito-urinary tract revealed that the right kidney was flabby and small (Fig. 2). Section showed it to consist of very remarkably dilated calyces within a 3 mm. shell of probably non-functioning cortex. The left kidney also showed a remarkable degree of hydronephrosis but there was an area approximately 4 cms. in diameter which was probably viable renal tissue. There was remarkably little evidence of infection, although there was an extensive peri-capsulitis bilaterally. Both ureters were dilated from kidneys to entrance into bladder, being about 1½ cms. in diameter.

The bladder wall was hypertrophied and the mucosal surface showed scattered pinkish areas of ulceration. The trigone was longer than normal but exhibited the normal relationships. The ureters opened into the bladder about 4 cms. above the verumontanum. The internal urethral orifice and prostatic portion of urethra was ballooned out and the lateral lobes of the prostate bilaterally extended far above the trigone region. This all suggests that the trigonal area has been pushed down through pressure of a distended bladder. The posterior portion of the prostatic urethra showed a small valve bilaterally which seemed to be an extension of the verumontanum (Fig. 3). There was in addition an outpouching of the urethra above the congenital valves described, which extended both dorsally above the urethra for a distance of about 2 cms. and above and posterior to the bladder for a distance of about 1½ cms. This outpouching is 2 mm. in diameter.

Case 3. W. M., male, black, age 15 days. Weighed 4 lbs. 10 oz. at birth. Gained to 4 lbs. 15 oz. in first 4 days and remained at that weight.

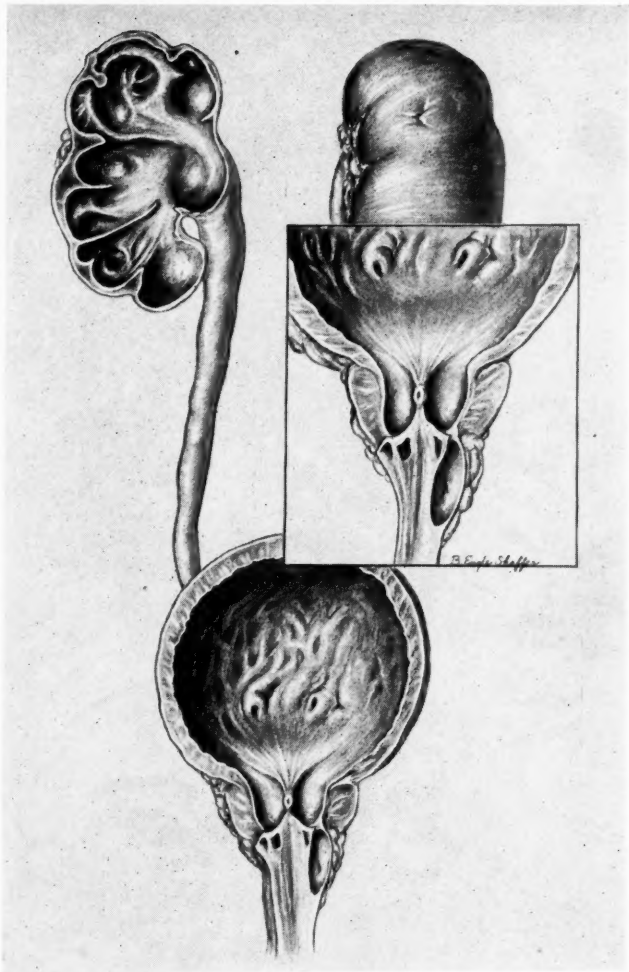

Fig. 2. A typical arrangement of type 1 is demonstrated in case 2. Note the abnormal position of the ureteral orifices with associated dilitation of the ureters and kidney structures.

On the eighth day the abdomen was firm. The child was irritable and appeared malnourished in spite of weight gain. Urination of small amounts was accomplished with considerable straining. The abdomen remained large. The child was catheterized on the 12th day and 70 cc. of clear urine was removed. Following catheterization the patient was comfortable. On the 13th day small amounts of urine were voided. The abdomen was still firm and gave the impression of a mass in lower abdomen, below umbilicus. On the 14th day, the abdomen was markedly distended. The child was catheterized and 200 cc. of concentrated urine was removed. The urine was slightly bloody. Blood urea nitrogen was 80 on the day of his death.

Autopsy revealed: Congenital valves of the posterior urethra type 2. The valves appeared as thickened fibrous bands extending from the verumontanum to the outer margin of the vesical orifices (Fig. 4). The bladder was greatly thickened, and dilated. The ureters were greatly enlarged and tortuous. The renal pelves and calices were greatly

dilated. There was considerable thinning of the renal parenchyma.

The original description of the condition is lost in obscurity. However, Morgani, in 1717 is credited with having presented the first anatomical description of this anomaly, al-

Fig. 3. Photomicrograph of valve leaflet. The low-power view shows that the valve is composed of collagenous fibrous tissue, which is moderately edematous. It is poorly vascularized, although toward one edge there is a dilated vessel surrounded by inflammatory cells. There is an indistinct covering of flattened and low cuboidal cells.

though the case report could not be found for verification. Langenback is credited with having described the pathological findings in 1802. Guthrie and Velpeau working independently reported in 1832 the effects of the urethral obstruction on the upper urinary tract. The first clinical recognition of the anomaly was reported by Eigenbrodt in 1891. Young, in 1912 first observed cystoscopically the formation of congenital valves and in 1913 he

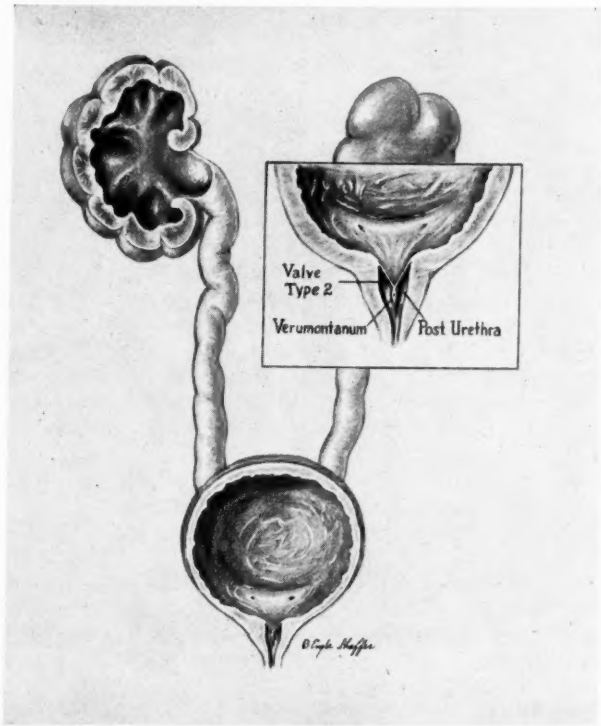

Fig. 4. The autopsy findings of a 15 day old infant dying of uremia. Note the formation of the valve leaflets in a classical type 2 formation.

was the first to treat the condition surgically. Since Young's original work numerous surgeons have been able to apply the surgical principles outlined by him with satisfactory results.

Young classified valves of the posterior urethra into three types (Fig. 5). Each type was classified according to the relationship of the anomalous leaflets to the verumontanum. The most frequently observed type of congenital valve is attached to the anterior end of the verumontanum and extends to the lateral walls of the urethra (Type 1). Extension of the valve leaflets from the posterior margin of the verumontanum to the bladder outlet is also described (Type 2). Another type (Type 3), may be totally independent of the verumontanum occluding the urethra as a partial or complete diaphragm or iris and may be situated either anteriorly or posteriorly to the verumontanum in any site of the prostatic urethra. There are many variations in the structural position and contour of congenital valves producing infravesical obstruction. An extreme variation of type three was observed in one of the cases presented. Case 1 (Fig. 2).

In this case the urethra penetrated through the verumontanum to open on its superior surface within the dilated posterior urethra. The hypertrophied verumontanum was located on the floor of the greatly dilated posterior urethra. The urethra was completely closed anteriorly. An instrument introduced through the urethral meatus would pass into the dilated posterior urethra through the sinus in the verumontanum.

ETIOLOGY

The etiology of congenital valves of the posterior urethra is unknown. There are several theoretical etiological suggestions but none of the apparent explanations accounts for all types of valve formation. The explanations most often discussed are four in number.

1. Tolmalschew believed that the valves are due to enlargement or modification of the folds and ridges normally present in the prostatic urethra.

However, as pointed out previously by other investigators, hypertrophy of the folds and ridges normally found in the urethra could account for types 1 and 2 but not for type 3. It is highly probable that the influencing factors of such anomalous formations are not always the same due to the wide variations of contour and position and construction of the valves.

2. Bazy believed that congenital valves were due to the persistence of the urogenital membrane.

3. Lowsley believes the valves are due to the anomalous development of the Wolffian or the Mullerian ducts.

4. Watson believed that they are due to attachment or "fusion of the tip of the colliculus to the roof of the urethra."

It may be seen that there exists no unanimity of opinion as to the etiological factors productive of these anomalous formations. Regardless of the etiology or the type of formation, the symptomatology presented by patients having such an anomaly is that of definite infravesical obstruction.

PATHOLOGY

The congenital condition of the posterior urethra is that of deep folds of tissue covered with mucous membrane. The pathological changes of the posterior urethra are those of dilatation behind the obstruction with varying destructive changes in the upper urinary tract. The formation of these cusps is such that instrumentation or catheterization is readily possible yet due to structural contour of the leaflets definite impediment to normal urinary flow results. With the iris type (Type 3), complete obstruction to instrumentation is usual. In this type the fenestra or opening may be so minute that even the introduction of a filiform bougie is impossible. It is believed that Case 1 of our series is a variation of this type, although the introduction of instruments was readily accomplished.

Unfortunately the pathological changes of the urinary tract are not limited to the posterior urethra. As the result of obstruction the posterior urethra becomes dilated. The bladder wall, early in the progress of the disease, shows hypertrophy with extensive trabeculation and inflammatory change. The increasing back pressure, as the bladder fails to overcome the resistance of the valves, causes dilatation of the ureters and renal pelves eventually producing bilateral hydroureter and hydronephrosis. The weight of the dilated ureter causes it to sag resulting in folds, kinks and angulations. Ureterovesical incompetency permits back pressure to be exerted directly on the renal parenchyma. Infection is inevitable. It has been repeatedly demonstrated and it cannot be overemphasized that stasis of urinary flow is the most frequent predisposing cause of infection. In the presence of congenital urethral valves, stasis of urinary flow and residual urine are apparent from the time of the first urination, so that infection invariably and inevitably becomes an important factor of the condition.

The life expectancy of patients with valve formation is usually short and is generally considered to be under 10 years. The pathological changes in the infant urinary tract may be so extreme in utero that death results at birth or shortly after birth as shown in one of our cases (Case 3). However, the manifestation of posterior valves may not become evident or too serious in extent until later in life. The age of one of our cases was 19 and presented a history of urinary disturbance beginning in early childhood.

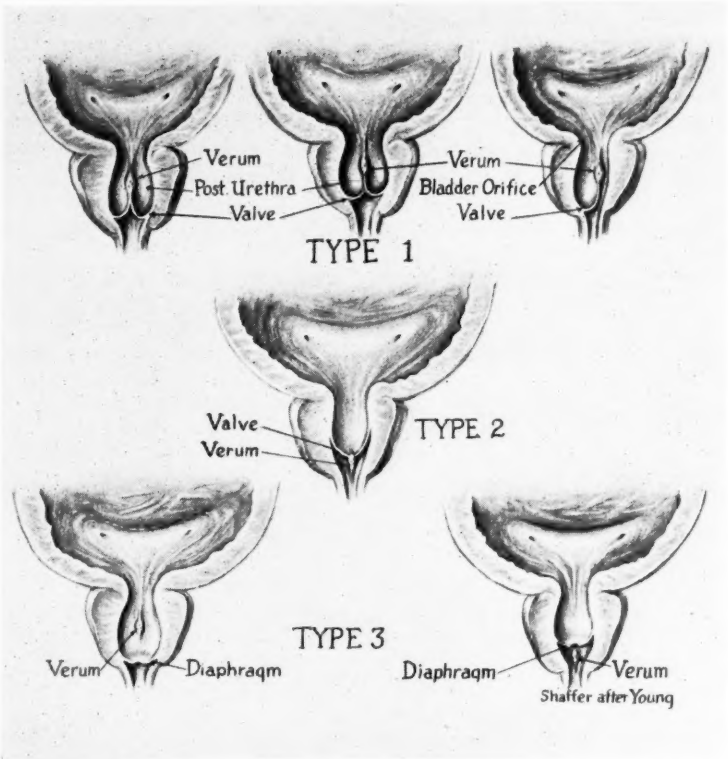

Fig. 5. Valves of the posterior urethra as classified by Young into 3 types. Type 1 is the most frequently observed type. The leaflets in this type are attached to the anterior end of the verumontaum. In type 2 the leaflets extend from the posterior margin of the verumontanum to the bladder outlet. Type 3 is described as a partial or complete diaphragm which may be situated either anteriorly or posteriorly to the verumontanum.

SYMPTOMS

The symptoms of posterior urethral valves are not always definite but are always suggestive. Any one of four symptom complexes may predominate: (1) Urinary disturbance, (2) urinary infection, (3) renal insufficiency, and (4) gastro-intestinal symptoms.

1. Urinary Disturbances: Frequency of urination is the most common symptom and is usually present from birth. Frequency of urination may become more intense as infection intervenes and increases.

Urinary dribbling or paradoxical incontinence becomes evident as the chronic retention is established. The distended bladder may be distinctly palpable suprapubically. In one of our cases, (Case 1), an elongated protuberance extended to the level of the umbilicus and was first thought to be a cyst of the urachus. As the chronic retention continues, the patient is continuously wet and may be considered as having eneuresis. Campbell cites nine cases that were considered as having eneuresis, but which were proven on study to have valve formation.

Difficult urination or dysuria is common and results from the obstruction produced by the valve formation. The small, hesitant, dribbling urinary stream passed with difficulty and straining is usually apparent and is a pertinent symptom of congenital valves of the posterior urethra.

Pain is frequently manifested by the crying, straining infant during urination. The chronically distended bladder produces lower abdominal pain as pressure by the abdominal muscles is increased in an attempt to urinate. Pain in the loin frequently occurs as the result of ureteral and pelvic dilatation and distention which is so frequent as the condition advances. Pain in the renal area during urination is suggestive of ureteral reflux and is a symptom not infrequently observed. It is due to the increased intrapelvic pressure through the widely dilated and incompetent ureterovesical sphincter at the time urination is attempted.

Hematuria, although not constant, may occur in varying amounts and should be regarded as an important symptom should it occur.

2. Urinary Infection: Infection of the urinary tract is inevitable and may be expected in every instance of posterior valve formation. Chills and fever with increased urinary frequency are common. The stasis of urinary flow and the dilated atonic ureteral and vesical muscular mechanisms are ideal factors favoring infection. In review of the histories of cases in the literature and those personally observed "chronic pyelitis" or "recurrent pyelitis" was commonly noted. The urine cultures of the cases reported were not unusual but rather those organisms commonly seen in urinary tract infection were isolated.

Acute accerbations of the urinary tract infection are common in the presence of acute upper respiratory infection. Following subsidence of the acute phase of the accerbation pyuria exists and remains in spite of medicinal therapy.

3. Renal Insufficiency: Renal insufficiency occurs in varying degrees as the destructive renal processes advance. As renal function diminishes, the signs and symptoms of toxic absorption increase. Blood urea nitrogen retention is increased and phenolsulphonphthalein excretion is diminished.

The clinical picture presented is not unlike that seen in advanced prostatism of later life. As the renal function continues to diminish the symptoms of uremia become apparent. Unless relieved, death is inevitable. If renal destruction is great it is doubtful that more than paliative or temporary restitution can be accomplished by any means or procedure. However, if corrective treatment is instituted early it has been most conclusively demonstrated that normal advancement of life and growth may be expected in some instances, although generally the condition presents a grave prognosis.

4. Gastro-Intestinal: Symptoms referable to the gastro-intestinal tract are common and may be extreme. Anorexia, nausea, vomiting, constipation or diarrhea are frequently seen. These symptoms may be so intense as to overshadow the urinary symptomatology.

Kretchmer and Pierson cited a case which was examined after death following pyloroplasty in which all symptoms during life were gastro-intestinal. Campbell cites another case in which constipation was extreme and resulted from compression of the rectum by the distended bladder. Failure to gain weight or even continued loss of weight presents a definite problem of management particularly during infancy and early childhood. The individual 19 years of age herein reported as Case 2 was noted to be small, stunted, and frail in stature with an unstable gastro-intestinal tract and a "picky" appetite and was also subject to frequent attacks of upper respiratory infection.

DIAGNOSIS

The diagnosis may be difficult or confusing. Complete urological examination offers the only possibility of establishing an accurate and true diagnosis. A complete urological study of the correlation of a carefully elicited history, physical, roentgenological and cystourethroscopic examination. Differential diagnosis must exclude hypertrophy of the verumontanum, fibrosis of the vesical neck, neurogenic bladder, chronic nephritis and polycystic disease of the kidney. The history of difficult, painful urination or straining at urination which has existed is usual and the distended bladder may be readily palpable.

In all three of our cases the distended bladder was palpable suprapubically. The kidneys and ureters may be palpable in advanced cases. Young and also Campbell have reported having palpated a greatly dilated ureter.

Roentgenographic studies offer visual evidence of the pathological changes in the urinary tract. Intravenous urography may or may not offer evidence of disease. This is particularly true in advanced renal destruction when the kidneys are unable to excrete sufficient contrast medium for visualization. Visualization of the entire urinary tract is usually accomplished at the time of cystography.

The cystograms usually reveal an irregularly enlarged bladder. The upper urinary tract on one or both sides is usually outline by reflux of the radio-opaque medium through incompetent uretero-vesical sphincters. The characteristic funnel-shaped dilation of the bladder outlet and posterior urethra extending to the obstruction is usually evident. Retrograde pyelography is seldom necessary in the presence of such concrete evidence demonstrated during cystography.

CYSTOURETHROSCOPIC EXAMINATION

Cystourethroscopic examination is usually a relatively easy procedure and assures definite informative data of the presence of congenital valves. The characteristic pathologic dilatation of the posterior urethra readily permits visualization. The valves or cusps may be observed as the irrigating medium is permitted to flow through the instrument into the urethra. As the cystoscope is advanced, the greatly dilated vesical orifice may be observed.

Further observation of the bladder reveals the trabeculated wall, the presence or absence of diverticula or calculi and the usually widely dilated ureteral orifices may be noted. Difficulty of observation may be experienced. In Case 1 of our series, the cystoscope entered the greatly dilated posterior urethra at a very acute angle through a sinus which penetrated the verumontanum; the intra-ureteral ridge was so markedly hypertrophied that visualization of the bladder was impossible. However such difficulty of examination is exceptional if the urethra will admit the passage of the cystoscope.

TREATMENT

It is imperative that slow decompression be done and stabilized urinary function is established before any surgical procedure is contemplated. Continuous catheter drainage is to be preferred to cystotomy although the latter procedure may be instituted because of the difficulty of retaining a catheter in the very young. Preliminary drainage may of necessity be continued for days, weeks, or even months until renal function returns to normal or approximately normal. Following stabilization of the urinary function, destruction of the valves and relief of the obstruction may be done. Transurethral destruction may be accomplished by suprapubic approach. Following destruction of the valves and the elimination of the obstructing factors, careful, meticulous pediatric feeding and observation are necessary as the prognosis greatly depends on the extent of renal damage and the patient's ability to assimilate the food given him.

SUMMARY

Congenital valves are undoubtedly not as infrequent as the sparsity of cases would lead us to believe. Obviously every male child with eneuresis is not a behavior problem nor is every instance of "pyelitis" an isolated infection of the kidney. However, every male child suffering with urinary difficulty, eneuresis or chronic infection of the urinary tract should be given the benefit of complete urological examination. The diagnosis of congenital valves is confirmed by cystourethroscopic and roentgenological examination.

RIASSUNTO

Valvole congenite non sono cosi' rare come si potrebbe dedurre dalla scarsita' della letteratura sull'argomento. Ecco perche' l'A. ritiene che ogni bambino affetto da disuria, da enuresi o da inferioni croniche delle vie urinarie debba essere sottoposto ad un completo esame urologico. La diagnosi di valvole congenite viene confemata da un controllo cisto-uretroscopico e radiografico.

SUMARIO

Las valvulas congenitales de la uretra posterior indudablemente no son tan raras como la esparcidad de los casos lo hace a uno creer asi. Indudablemente no todos los casos de eneuresis en el muchacho son problemas sicologicos ni tampoco son todos los casos de pielitis casos isolados de infection renal. Sin

embargo todos los muchachos que sufren de dificultades de la micturicion, eneuresis, e infeccion cronica del conducto urinario deben de darseles el beneficio de un examen urologico completo. El diagnostico de valvulas congenitas se confirma generalmente por la cisto-uretroscopia y la radiologia.

SOMMAIRE

Les valvules congénitales ne sont pas aussi rares que l'on croit. Naturellement, chaque enfant mâle ayant de la difficulté à uriner et chaque cas diagnostique "pyelitis" n'est pas une infection isoleé du rein. Néanmoins chaque enfant mâle ayant de la difficulté à uriner ou présentant une infection chronique de voies urinaires, doit avoir le bénéfice d'un examen urologique complet. Le diagnostic des valves congénitales est confirmé par un examen cystouréthroscopique et roentgénologique.

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CORRECTION

The article appearing under News Notes, on page 204 in The Journal of the International College of Surgeons, No. 2, 1949, should have read as follows:

Professor Dr. Manuel A. Manzanilla, of the Faculty of Medicine of the University of Mexico, was presented with the decoration of the National Order of Merit, "Carlos J. Finlay," which was conferred upon him by His Excellency, the President of the Republic of Cuba.

The Role of Ultraviolet Blood Irradiation Therapy* *Knott Technic* in Surgery

R. C. OLNEY, M.D., F.I.C.S.**
LINCOLN, NEBR.

ONE of the valuable contributions to medicine in recent years has been the development of the *Knott Technic* of ultraviolet blood irradiation therapy.

To date there have been published some thirty articles dealing with the subject, as a result of over 60,000 treatments given throughout the United States in the past 15 years with no deleterious effects having been noted.

This procedure involves an entirely new principle in the application of ultraviolet ray for therapeutic purposes, and in order to present the subject clearly and concisely, I have chosen to discuss it in the following manner:

First, what is it? Second, how does it act? Third, what are its uses? These are the usual questions asked.

WHAT IS IT?

After many years of intensive work Knott discovered a new and extremely valuable phenomenon, which is: that a definite short exposure of selected ultraviolet rays properly impinged upon a definite amount of the *patient's blood* produces certain reproduceable reactions which combined, greatly increase the patient's resistance.

The result of this procedure is not the sterilization of the blood by the bacteriocidal action of ultraviolet ray, but the marked stimulating effect upon the resistive forces of the patient, which is vastly more valuable.

This method of applying ultraviolet rays to the blood and the amount of blood so exposed to the rays, and the time factor of such exposure has been carefully worked out and reduced to a scientific formula, that when used according to the formula, reproduce within the patient certain definite reactions.

This procedure in its entirety has become known as the *Knott Technic* of ultraviolet blood irradiation.

It consists of the withdrawal and citration of an exact amount of the patient's blood, which is 1½ cc. per pound of body weight. This citrated blood is then returned to the patient through the Knott Hemo-Irradiator, a precision machine which automatically exposes the blood to ultraviolet ray at close range at the rate of 10 cc. in 10 seconds, with a turbulent movement of the blood column so that each particle of blood is exposed only for a fraction of a second.

The blood returns immediately to the patient through the same intravenous needle through which it was withdrawn.

The time required for this procedure is about 15 to 20 minutes.

HOW DOES IT ACT?

Application of ultraviolet blood irradiation in accordance with the *Knott Technic* produces within the patient certain definite reactions consistently:

A. An increase in the oxygen factor of venous blood as determined by the Van Slyke Technic (G. P. Miley and others).

A long series of cases of known low-venous oxygen values were treated and there was found a consistent rise in venous oxygen values ranging from 50 percent to as high as 300 percent.

(The oxygen increase was verified by experiments carried out by the United States Naval Air Service in a low pressure chamber study of anoxia and bends susceptibility.)

The value of a safe method of effecting and maintaining an increase in oxygen exchange factor in the blood stream of a patient is well known.

B. A rapid rise in the opsonic index.

Following treatment the phagocytic action of polymorphonuclears is markedly increased.

The original work showed an increase up to 50 percent in the number of bacteria ingested in the cell.

* Presented at the Thirteenth Annual Assembly of the United States Chapter of the International College of Surgeons, St. Louis, Nov. 15-20, 1948.

** President, American Blood Irradiation Society.

Later work performed by M. A. Sullivan and Morton Beroza have established the increase in bacterial ingestion from 38 percent to 78 percent.

Such an increase in the opsonic index of blood is valuable in the treatment of infections.

C. Vasodilatation and increased capillary flow.

There is marked evidence of peripheral vasodilatation.

D. There is a profound effect upon toxic patients with relief of toxic symptoms.

This phenomenon is most consistent.

E. Chylomicron studies in critically ill patients show rapid return of brownian movement.

F. Extensive tests of the effect of short-time irradiation on blood and biochemical compounds have shown that beneficial alteration chemically of certain important constituents of the blood take place following exposure by the *Knott Technic* of ultraviolet blood irradiation, e.g., adrenalin, dihydroxyphenylalanine, cysteine hydrochloride, glutathione and ergosterol.

WHAT ARE ITS USES?

Wherever increased blood oxygen, increased phagocytosis and vasodilatation will benefit a patient, this therapy is useful.

Its uses in medicine are just as important as those in surgery, but this discussion is confined to its role in surgery.

In using this one must continually keep in mind the fundamental effects of this therapy as a valuable supportive measure, and not think of it as applied to certain diseases as a specific therapy.

This is one of the most valuable aids in handling serious surgical cases. Our experience covers over 800 patients so classified.

There is marked reduction of swelling and pressure in affected parts, with relief of pain and rapid restoration of function in the affected organs.

In general peritonitis and postoperative ileus, with the patient cyanotic, rapid pulse, greatly distended, vomiting, no bowel action from any means, if ultraviolet blood irradiation is given, the cyanosis is relieved promptly, intestinal tone is rapidly regained, and in from four to twelve hours the patient will usually have three or four defecations and elimination of large amounts of flatus, will stop vomiting, the distention is relieved, and the abdomen becomes soft.

If this result is not obtained and the patient proves to have a mechanical obstruction, the abdomen should be opened. Following this treatment the patient's general condition is greatly improved and this surgical attack can be done with much greater safety.

Patients with an acute surgical abdomen, such as ruptured ulcer, acute severe gallbladder disease, acute severe pancreatitis, and similar conditions, when given this therapy at once, rapidly begin to show relief of serious symptoms.

Then if desired, the patient may be operated immediately and the operative attack is withstood much better.

The treatment should be repeated the day after surgery.

If preferred, after the first treatment the patient may be watched for a few hours, and in cases in which there is not a ruptured viscous, appendicitis, or such an obvious acute surgical emergency, the acute symptoms will begin to subside rather rapidly, and in the case of the acute gallbladder or acute pancreatitis, etc., the patient may be spared an operation.

In gallbladder disease this therapy is extremely valuable. My own series covers over 400 cases.

The problem of the acute gallbladder is greatly reduced, since in patients with acute severe gallbladder disease, in most cases symptoms will subside rapidly, vomiting cease, and the critical attack will be rapidly averted. There is reduction of swelling and pressure in the biliary ducts—promoting drainage. If necessary, later, the patient may or may not have an operation.

If symptoms do not subside in two or three days, the patient with a gangrenous gallbladder or an impacted stone with gangrenous duct may be operated on immediately, and it is surprising how well these patients withstand this surgery, having blood irradiation before the operation. Usually cholecystectomy can be performed instead of cholecystostomy.

Patients having had the gallbladder removed, who continue to have biliary attacks with pain, vomiting, clay colored stools, etc., although on good medical and dietary management, will get complete relief in most cases by ultraviolet blood irradiation therapy in addition to the medicine and dietary treatment. I have had over 100 such cases of from two to 25 years duration with complete relief of symptoms in 90 percent.

In non-specific pelvic infection or cellulitis, both acute and chronic, this has proven to be of great value. I have had over 600 patients in this group.

In acute, severe, pelvic cellulitis and puerperal sepsis patients respond promptly with marked relief of pain, swelling and temperature, and recovery is hastened in most instances without surgical drainage.

In chronic pelvic infection or cellulitis patients with massive inflammatory disease without definite abscess or cyst improve markedly with this treatment.

The swelling, pain and tenderness disappear and in a reasonably short time most of these cases return to normal.

Severe lymphangitis, adenitis, and cellulitis respond promptly with rapid reduction of pain, redness and swelling and without localization and surgical drainage in many cases.

In many postoperative complications such as postoperative pneumonia, atelectasis and embolism, the supportive effect of ultraviolet blood irradiation is a very valuable adjunct.

There is marked relief of pain and cyanosis with a rapid stimulation of the general resistance of the patient.

Thrombophlebitis and phlebothrombosis likewise respond remarkably to this treatment with relief of pain, swelling, and a rapid resolution of the process without embolism in a high percentage of cases.

The ideal method of using this therapy in *elective* cases requiring serious surgery, such as total hysterectomy, serious biliary surgery, is to give the treatment before and after operation.

Sometimes two or three treatments in the two, three or four weeks before operation.

Usually, however, one treatment the day before and one the day after surgery.

When so handled these patients seldom vomit, *rarely require suction drainage of the G-I tract.*

The abdomen is seldom distended.

Patient usually expels flatus without assistance.

They are seldom toxic, move and turn easily, require less opiate, I.V. fluids, and transfusions.

Valuable gastric and duodenal secretions are retained and electrolyte and fluid balance is easily maintained.

Complications such as thrombophlebitis, phlebothrombosis, embolism, pneumonia, etc., are greatly reduced and if they occur, are greatly benefited by ultraviolet blood irradiation therapy.

Mortality and morbidity are greatly reduced.

SUMMARY

In conclusion, it is important to emphasize that the *Knott Technic* of ultraviolet blood irradiation is a valuable supportive measure, the effects of which are the marked stimulation of the resistive forces of the patient, and not a specific therapy.

These effects are: 1. Increased blood oxygen. 2. Increased phagocytosis. 3. Vasodilatation.

In all of our work we have used control cases as nearly as possible in all series, selecting cases as nearly identical to those treated, for control purposes.

RIASSUNTO

L'irradiazione del sangue con raggi ultravioletti (tecnica di Knott) non rappresenta una terapia specifica, ma ha principalmente lo scopo di aumentare le difese organiche del paziente. Gli effetti del sangue irradiato consistono: in un'aumentata ossigenazione del sangue; in un'accresciuta fagocitosi; in una vasodilatazione. Per definire meglio gli effetti teraupetici, l'A. ha selezionato casi di controllo quasi identici a quelli trattati.

SUMARIO

En conclusion, la terapeutica por irradiacion ultravioleta de la sangre, segun el metodo de Knott, es de valor como medida suportiva. Su efecto es el estimular los poderes de resistencia del paciente, y por lo tanto no es terapeutica especifica.

SOMMAIRE

En conclusion, il importe de comprende l'utilité de radiation ultra-voilette du sang (Knott technique) et d'en peser les grands avantages. Ces irridations augmentent la résistance du malade.

Ce n'est pas un traitement spécifique.

Il produit une augmentation:

1. De l'oxygène dans le sang.
2. De la phagocytose.
3. De la vasodilatation.

Dans tous nos ouvrages, nous avons employé des cas contrôlés aussi proches que possible des cas aussi identiques que ceux que noux traitions.

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Atrophy of the Vaginal Mucosa
A Clinical Study of Thirty-Eight Cases*

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ACCORDING to Robert Myer, as quoted by Novak,[1] the vaginal epithelium is no longer considered as part of the mullerian system, still it is clearly under the influence of the ovarian hormones. Atrophy of the vaginal mucosa almost always results from ovarian deficiency and a good example is found in the so-called senile vaginitis. As will be shown later, atrophic changes of the vaginal epithelium may take place during any period of a woman's life and is by no means limited to the senile.

Atrophy of the vaginal mucosa thus far has been discussed little for manifold reasons. In the first place, as a sign it is frequently overshadowed by other important findings; so much so that in the discussions of such clinical entities as Simmond's disease, atrophy of the vaginal mucosa is scarcely touched upon, although in some such cases genital atrophy may not even take place.[2] Secondly, uncomplicated atrophy of the vaginal mucosa usually causes little or no symptoms. Thirdly, sporadic cases of senile vaginitis do not seem to arouse much interest as we almost always take it for granted that the picture is just what we would expect of that age. Actually atrophy of the vaginal mucosa deserves more attention than it has been hitherto given and is, as will be shown later, helpful to the gynecologist in many ways.

During the last six years the writers devoted quite some time and effort to make periodic observations on patients with atrophic changes of the vaginal mucosa, and followed them up for periods varying from three to five years. Altogether 38 cases were studied, those that have failed to reach this time limit have all been discarded.

CLASSIFICATION

From the clinical viewpoint, atrophy of the vaginal mucosa can be divided into four groups. The post partal, the premenopausal, the senile or post menopausal and the artificial which includes both surgery and irradiation. A fifth group may be added, that is, atrophy following debilitating diseases or poor nutrition only they are much in the minority. The distribution of the cases is shown in Table 1.

TABLE 1

Type of Atrophy	Post Partal	Premeno-pausal	Senile	Artificial Surg.	Artificial Irrad.
Number of cases	19	8	6	2	3

CLINICAL OBSERVATIONS

As far as the local changes are concerned all groups present more or less the same picture. We shall first proceed with the general picture of atrophy and point out the minor differences in the discussion of the separate groups.

The earliest sign of atrophy of the vaginal mucosa is a smooth and pale outlook of the whole canal which may be devoid of rugosae, especially over its upper third. This is soon followed by the appearance of submucous red patches (telangiectatic spots), first over the portio vaginalis of the cervix, then the upper part of the vagina. These spots are found most frequently in the premenopausal and senile groups. There are no cracks over these spots, the overlying mucosa being intact. In the senile group red streaks and cracks may be found over the fornices.

When the upper vaginal canal and the cervix are smeared with Lugol's solution (Schiller's test), one may see over the uniformly mahogany stained cervix and upper vagina, in contrast, greyish white, oval shaped patches that fail to take up the stain.

The mucosa covering these patches appear intact. The patches may become confluent and

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are located mainly over the posterior cervical lip and the posterior fornix. The epithelium over the telangiectatic spots, on the other hand, takes up the stain, and if one waits long enough, these spots may stand out darker than the rest of the parts. This contrast in stain takes place most vividly in the premenopausal group, but is not present in every case.

As time goes on the vaginal canal gradually yet definitely narrows down, with its walls ever increasing in rigidity. Thickening takes place mainly in the submucosa; the fornices, especially the posterior one, quickly shallow out.

SEPARATE CONSIDERATIONS

The Post Partal Group: Most of the patients in this group came to us rather late. The earliest patient was one and one half years, and the latest, seven years after parturition. The whole genital tract, including the vulva, appears atrophic and the uterus is either super or hyperinvoluted. The vaginal canal is narrow and in some cases it may feel like a rigid tube. Telangiectatic spots, red streaks or cracks over the mucosa are not common. However, when the mucosa is pressed hard with the vaginal speculum, spotted submucous hemorrhages may be seen. Severe cases are usually associated with superinvolution, the cold syndrome, etc., the classical picture has been well described by Sheehan and McLetchie.[3] The vaginal canal narrows down rather quickly and in less than three years' time (after parturition) coitus may become impossible. Finally the whole canal becomes a rigid narrow and fairly straight tube, further trauma such as from coitus and friction does not seem feasible, and coalescence is rare.

In the mild forms the patients show little or no signs of endocrine disturbance other than amenorrhea and the uterus may be only slightly hyperinvoluted. The vaginal canal narrows down only very gradually and rigidity is not marked. The atrophied mucosa however, is constantly exposed to trauma from coitus and frequently rubbing of the walls against each other at the mid or lower portion of the vagina where approximation is easy. Coalescence may often be the end result.

A typical history of this group, including both mild and severe forms, is prolonged and continuous amenorrhea years after a childbirth. The labor may or may not have been difficult, but the patient had either suffered from much blood loss or else the puerperium was febrile and stormy. The patients are usually young, and the clinical pictures they present are pathetic. Table 2 shows the age distribution between the two forms. Three of our severe cases fitted pretty well with the clinical picture as described in detail by Sheehan and McLetchie, but none of the patients showed any crisis of attack that these authors described in their report.

TABLE 2

	Number of cases	Age					
Severe	5	36	23	22	26	23	
Mild	11	28	25	21	23	23	35
		30	35	29	26	38	

A somewhat allied group is marked by ever increasing obesity following childbirth, with infrequent menstruation. The uterus may be undersized but the vaginal canal appears only slightly atrophic. This group is not included in our study.

Atrophy After Prolonged Dystocia: Neglected cases of dystocia, where the fetal head has been kept in the vagina for days and the whole birth canal extensively damaged by fruitless instrumentation or manual manipulation, may result not only in marked atrophy of the vaginal mucosa but also a bizarre derangement of the anatomy of the pelvic organs. This type of atrophy has a much better prognosis once it escapes the fate of the above mentioned forms, which it usually does. It rarely lasts more than eight months.

Occasionally one may pick up a case of fairly marked atrophy of the vaginal mucosa during a routine post partal examination, mindful, of course, of the usual degree of atrophic changes during the first few weeks post partum. The cause for atrophy in such cases is obscure, and the picture improves readily with estrogens. Table 3 shows the factors that may lead to post partal atrophy and the distribution of our cases therein.

TABLE 3

Infection	9
Hemorrhage	4
Tuberculosis	1
Poor nutrition	1
Damage from prolonged dystocia	1
Unknown	3

Atrophy During Lactation: This form of atrophy is also associated with amenorrhea so long as lactation continues. Once the patient stops nursing her baby the atrophic picture immediately improves. Should lactation be prolonged for more than two years which is not uncommon in China, atrophy will remain more or less stationary that long. What usually happens however, is that after four to six months of lactation, menstruation returns and the woman may keep on nursing her baby for a few additional months. The relationship between lactation and genital atrophy is a rather vague one.

The Premenopausal Group: This group is so named for want of a better term. Most of the patients in this group have passed their 40th year, thus approaching menopause. The vaginal canal is neither rigid nor narrow. Atrophy of the vaginal mucosa though less marked, is definite. Red patches (telangiectatic spots) are common but there are no cracks. These spots are located mainly over the cervix and upper vagina, seldom the lower third. Trauma from coitus or friction between the walls does not seem to have much effect on the integrity of the mucosal surfaces. There is no tendency toward coalescence. The patients usually come in with a bloody vaginal discharge and the clinical picture is that of slight atrophy plus some mild infection.

In the senile group the vaginal canal is narrow and shrunken, the mucosa may be smooth and shiny. Rigidity of the walls is less marked, and the canal is usually half plugged by either a cystocele or a rectocele or both. Linear cracks or red streaks may appear anywhere in the vaginal canal but they do not seem to have the same appearance as the telangiectatic spots found in the premenopausal group. Bleeding occurs on the slightest trauma from the vaginal speculum. The uterus is always small. Table 4 shows the age distribution among the premenopausal and senile groups in our series.

TABLE 4

Group	Age							
Premenopausal	44	50	47	41	37	42	47	43
Senile	66	74	51	54	71	75		

The atrophic picture following irradiation or surgery would seem to depend upon the amount of ovarian tissue destroyed or removed. Following radium application, the immediate picture is that of an irritation, atrophy does not set in until a few months afterwards. The walls would then gradually become rigid and close in from all sides. Cases of coalescence, apparently from constant friction between the opposite walls, before the atrophic picture is complete, have been observed.

Infection and Trauma: Atrophy of the vaginal mucosa if not complicated by trauma and/or infection, may not cause any local symptoms for a long time. Leucorrhea in the absence of infection is uncommon. The predisposing factors to infection are many, among which may be mentioned:

1. The act of coitus which is a constant source of contamination in addition to the trauma it incurs over the already thinned out epithelium.

2. Lowered bactericidal power in the vaginal canal.

3. Constant rubbing of the approximated surfaces against each other. Infection is invariably present in the premenopausal group, but is readily controlled.

Coalescence: This usually results from incomplete cornification of the vaginal epithelium and is the natural sequelae to trauma and infection.[4] Peculiar enough, it seldom takes place in the premenopausal group, wherein atrophy does not seem to play the major role. (This will be discussed later.) As mentioned before, trauma and infection will not have as much effect in the sense of destroying the integrity of the mucosa, as on the other groups.

Beginning coalescence is marked by formation of adhesions between the anterior and

posterior vaginal walls at a level slightly below the mid part of the canal, where constant rubbing of the approximated surfaces takes place most readily. Once formed, they can not be broken without tearing off a piece of the vaginal wall, which may cause quite some bleeding. These adhesive bands form almost along the same level but may start at two or three different spots. In about six weeks' time they join together to make the block complete. McLaren also made the observation that after radium therapy stenosis of the upper vagina was common, "occasionally accompanied by a circular occlusive band about two inches from the introitus."[5] In our series three cases in the post partal group and two in the artificial (irradiation) ended in complete coalescence.

The Cervix: The cervix in cases of atrophy of the vaginal mucosa as a rule, is small and free from erosions. The portio vaginalis feels hard and is covered with atrophic mucosa. In the premenopausal and senile groups there may be a few telangiectatic spots.

The Uterus: The uterus in the post partal group is either super or hyperinvoluted and is always amenorrheic. In the premenopausal group it is usually of normal size or slightly larger than normal. Menstrual disturbances such as irregularity, scanty flow and infrequent menstruation are common, rarely the flow may be excessive.

The Ovaries: In the premenopausal group the ovaries may feel cystic, in the rest of the groups they are hardly palpable.

The External Genitalia: Here again the premenopausal group shows the least deviation from normal. The rest of the groups almost invariably show scanty pubic hair and atrophic labia.

THERAPEUTICS

For the severe cases in the post partal group we used a polyglandular extract which contained a bit of everything, according to the labels. The mixture was of unknown potency and was given intramuscularly every other day in 10 cc. doses. This was supplemented with rather heavy doses of thyroid and estrogens. The immediate effect was quite good as far as improvement of the general symptoms such as lack of pep and the cold syndrome, etc. were concerned. Locally, the rigid vagina also loosened up quite a bit. However, there has never been any appreciable change in the size of the uterus and amenorrhea has been persistent all the way through.

For the mild cases of post partal atrophy, administration of the estrogens would enhance cornification so as to enable the mucosa to better overcome the effects of trauma from coitus and friction. In this way secondary coalescence may be prevented.

For the premenopausal group, administration of the estrogens with or without thyroid, never failed to bring the mucosa back to its healthy state. The bloody discharge stopped in a few days, and the cure in most cases seemed to be permanent. As the patients were mostly within the cancer age, and as the estrogens have been suspected as carcinogenic, the drugs were administered with the utmost precaution. Our best guide has been a definite picture of atrophy, preferably with telangiectatic spots.

For the senile group, administration of the estrogens may or may not yield immediate results. The treatment, to be effective, has to be intermittent if not continuous, which is definitely hazardous. Nevertheless, we used the estrogens rather freely on our cases.

We have no experience with the vitamins in the treatment of atrophied vaginal mucosa.

GENERAL DISCUSSION

Hypoovarian function with lowered blood estrogen levels has always been regarded as the logical cause for atrophic changes of the vaginal epithelium. This belief has been strengthened by the fact that in many cases the clinical picture improves rapidly upon administration of the estrogens. This is in general, quite true, but it does not necessarily follow that the incidence of atrophy of the vaginal mucosa should increase with age. Indeed, McLaren[5] stated that the majority of women who have passed menopause retain normal vaginal mucosa. Shute[6] also suggested the possibility of continuation of the estrogen cycle with occasional rises of its level after menopause. Both statements argue for our contention that atrophic vaginitis should not be limited to the senile. As the clinical picture is mainly one of atrophy and it effects

women of all ages the same way, there is really no necessity of recognizing senile vaginitis as a separate disease entity.

In the post partal group, with the most severe forms that are symptomatic of multiple endocrine deficiency, necrosis of the anterior pituitary as evidenced by postmortem findings should rightfully be considered as the etiological factor. With the less severe forms, in which the patients show no other symptoms than amenorrhea associated with atrophy of the vaginal mucosa, also perhaps a somewhat hyperinvoluted uterus, it would be difficult to say whether they are also due to necrosis of the anterior pituitary body but to a lesser degree, or to infections that have fatally damaged the uterus and/or the ovaries. The fact that infection alone may count for some cases of superinvolution, take for instance, gas bacillus infection as reported by Lennon and Williams,[7] would suggest that the damage may primarily be in the uterus. Since necrosis of the anterior pituitary can also take place during pregnancy,[8] one can not leave the anterior pituitary out altogether even in the presence of severe infections. The chances are both the anterior pituitary and the uterus may be primarily involved. Whether the same can be said of the ovaries or not remains to be seen.

It sounds logical to suspect that the cause of atrophy in the premenopausal group might be beginning ovarian failure which would eventually lead to menopause. Our observations do not seem to support this view. All of the cases responded to the estrogens readily, but continued to menstruate regularly years afterwards. In most cases the cure seemed to be permanent and we did not have to keep on with the drug for more than a few weeks either. We therefore suggest that in this group infection plays the major role. Additional estrogens merely help to restore the normal state of cornification which would render the canal more resistant to the invading organisms. That should not take too long.

In the senile or post menopausal group certainly the logical cause would again be lowered blood estrogen levels. Still senile vaginitis is a comparatively rare disease and if ovarian failure were common after menopause, that is, assuming that the ovaries are still the chief source of the estrogens, we should certainly see more of it. The reason why we do not is probably because that in most women who have passed menopause, estrogen supply has not been appreciably depleted. That again brings up the interesting question of cyclic ovarian activity after the menopause.[6] Such are high probabilities although substitution from the adrenals has been suggested.[9] McLaren's studies on the histology of the post menopausal vaginal mucosa and his conclusions thereof, i.e., most patients retain normal vaginal mucosa, further support this view. The therapeutic effects also seem to indicate that in the so-called senile vaginitis, the estrogens, wherever they may come from, have been appreciably decreased in amount.

On the other hand, Shute has pointed out that degenerative vulvovaginitis may be associated with either estrogen deficiency or estrogen excess.[6] We have not seen a case of atrophy that failed to respond to the estrogens, which of course, implies that all our cases belonged to the estrogen deficiency group. However, it has been our observation that atrophic vaginitis is seldom complicated by vulvitis. In some of our cases the vulva appeared wet and atrophic but signs of degeneration and inflammation were wanting. Here we must not forget, as Savill[10] has shown, how easily skin lesions over the vulva can be misdiagnosed. One should not wonder that many vulvar lesions can be associated with estrogen excess.

In case of atrophic vaginitis where the vulva is more or less spared, the assumption may be made that just as the uterus may need more estrogens than the vaginal mucosa for its development and function,[11] the latter might in turn, need more estrogens than the vulva for the same purposes. From this we may again infer that in such cases the estrogen level in the blood may become low enough to effect the vagina but not the vulva. Such are hazardous conclusions as we know very little about the relationship between the ovaries and the vulva. In kraurosis for instance, the best known form of vulvovaginitis, the use of the estrogens is by no means specific.[9] Moreover, kraurosis consists of a shrinking process that starts from the vulva and proceeds towards the lower end of the vagina

while atrophic vaginitis starts from the other direction. One process seldom extends to the realm of the other. They can hardly have the same cause. It is very likely that the cases described by Shute as degenerative vulvovaginitis are not identical with the pictures of atrophic vaginitis we have studied.

McLaren[11] stated that in case of atrophy the thinning out of the mucosa with added trauma would permit entrance of organisms. It is also our observation that uncomplicated post partal atrophy seldom causes any local symptoms. Leucorrhea in the absence of superficial infection or trauma is rare. Uncomplicated atrophy is usually discovered during gynecological examinations for prolonged amenorrhea following childbirth or during routine post partum check up examinations. In the premenopausal group a bloody vaginal discharge usually brings the patient to the doctor. The discharge comes from increased desquamation in the presence of some low grade infection. The blood stain probably comes from the telangiectatic spots that have broken down, which phenomenon is better observed in the senile variety.

The spotted greyish white patches that fail to pick up the stain in Schiller's test may deserve special comment. These patches have apparently lost their glycogen content. It is well to point out here that this finding is in line with the histology of post menopausal vaginitis as described by McLaren[11] who demonstrated that in such mucosa patches of superficial desquamation of epithelium are present. Intervening areas of apparently normal tissue with abundant glycogen may be seen. On the other hand, as depletion of glycogen is not uniform, this phenomenon might as well be considered as one form of varying tissue sensitivity to the hormones. This is highly conjectural and less likely. Anyhow the patches do not appear to be traumatic in nature. All of our cases that showed up these patches have been amenable to the estrogens. Incidentally, they all belonged to the premenopausal group.

Another interesting finding in this study is that complete coalescence following radium application takes place mainly in the aged. The younger patients seldom develop such a complication. Would it be possible that after the usual dosage of irradiation, the ovaries of the younger patients may possess better power of regeneration? Indeed pregnancy after as much as 2000 milligram hours of radium application has been reported.[12]

Our changed conception of the embryology of the vagina, that is the vaginal epithelium is not mullerian in origin, makes it difficult to understand why coalescence stops at about the level of the junction between the lower third and the upper two thirds. We formerly thought that this level would be where the uterovaginal canal and the urogenital sinus meet, also where the mullerian system ends. This can not be true. The alternative explanation would be that the level mentioned often marks the point of contact between the anterior and posterior vaginal walls and is constantly subject to trauma (friction), which eventually leads to complete coalescence. After atresia is complete, the lower third of the vagina and the vulva though spared in the process, remain atrophic, but the picture does not seem to become worse with time.

CONCLUSIONS

From the above it is evident that:

1. Atrophy of the vaginal mucosa if present, may help to rule out malignancy suspected of patients in the cancer age, when they complain of a constant bloody discharge.

2. Schiller's test, which is often used in the differential diagnosis of early carcinoma of the cervix, when done over the atrophied mucosa may need intelligent interpretation.

3. Early recognition of the condition in routine post partal examinations followed by prompt endocrine therapy will prevent further damages from trauma, infection and the sequelae therefrom.

4. The importance of proper management of labor in childbirth, to insure against excessive blood loss and post partal infections, need not be stressed here.

5. Senile vaginitis should no longer be considered as a separate disease entity.

SUMMARY

1. A study of 38 cases of atrophy of the vaginal mucosa was made.

2. A tentative classification of atrophy of the vaginal mucosa was suggested.

3. The clinical course and the important diagnostic features of each group were presented.

4. The etiology and treatment of each were briefly discussed.

5. The significance of atrophy of the vaginal mucosa was considered.

RIASSUNTO

Un'atrofia della mucosa vaginale, se presente, aiuta ad escludere una neoplasia maligna nelle pazienti che rientrano nell'eta' del cancro e che accusano una costante secrezione sanguigna. La prova di Schiller, spesso usata nella diagnosi precoce del cancro cervicale, richiede, un'interpretazione molto accurata se eseguita sopra una mucosa atrofica. Un precoce riconoscimento di questa condizione nelle visite post-partum, seguito da un'opportuna cura endocrina, puo' evitare ulteriori danni da traumi, infezioni e relative conseguenze. La vaginite senile non va piu' considerata come un'entita' morbosa a se'.

SUMARIO

Segun los autores la atrofia de la mucosa vaginal cuando esta se presenta ayuda a eliminar el cancer en casos sospechosos. La prueba de Schiller debe de practicarce con mayor diligencia, y su interpretacion debe de hacerse con mas cuidado en casos de atrofia de la mucosa vaginal. Es importante el reconocer tempranamente esta condicion haciendo examenes despues del parto para asi tratarla por la endocrinoterapia. No es necesario repetir la importancia que es menester el dar a todas las madres en cinta y durante el parto. La vaginitis senil no se debe de considerar como una entidad independiente.

SOMMAIRE

Quand l'atrophie de la muqueuse vaginale existe, on peut ordinairement, même si la malade est de l'âge cancéreux ou si elle se plaint d'un écoulement sanguin constant, éliminer le diagnostic de carcinome. L'épreuve de Schiller que est souvent employée pour faire le diagnostic différentiel dans le carcinome précoce du col uterin, fait en présence de la muqueuse atrophiée, demande une interprétation intelligente. Si on reconnait l'état à temps dans l'examen qui suit la délivrance, on peut à l'aide d'une thérapie endocrine, empêcher des lésions futures dues au trauma, à l'infection et aux séquèles de l'infection. Il importe de conduire l'accouchement de façon à eviter toute hémorragie excessive et toutes infections puépérales. La vaginite sénile ne doit pas être considérée comme une maladie séparée.

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The Management of the Rigid Hymen and Perineum Early in Marriage*

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NOT infrequently we are presented with the problem of a rigid, non yielding hymen and perineum in early marriage. Because of its alleged minor importance, it may be relegated to a secondary role in surgical gynecological judgment and management.

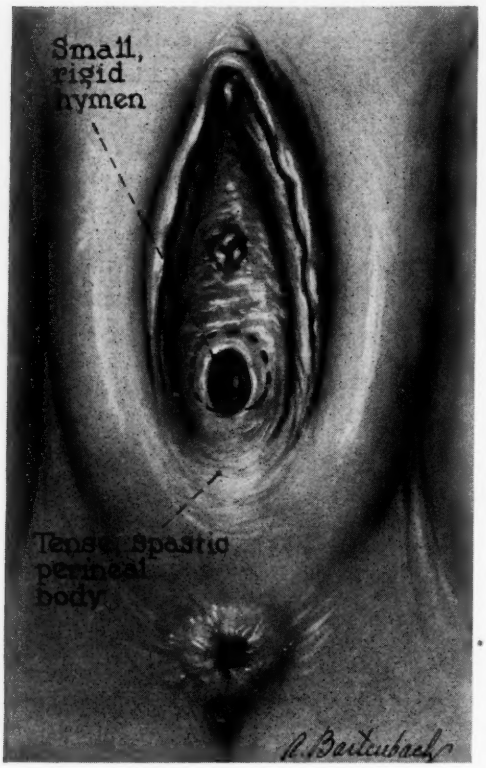

Fig. 1. Circumferential excision of hymen.

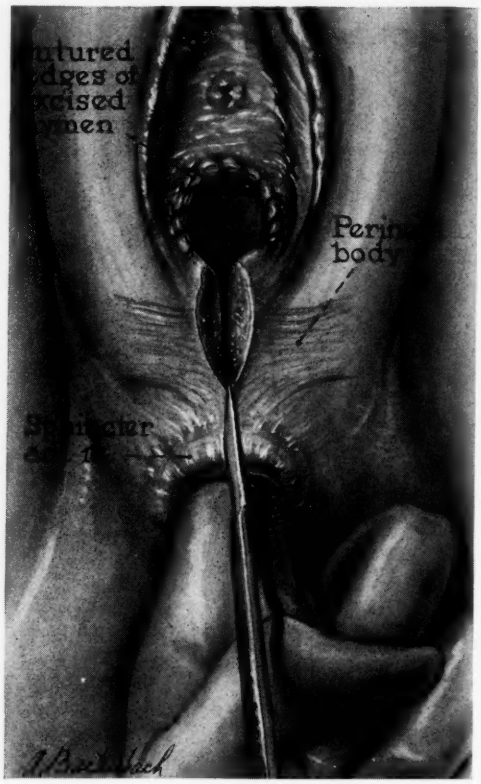

Fig. 2. Midline perineotomy with finger in rectum as guide.

In the past there were many different methods and various attempts were made to alleviate this condition; such as actual coitus, digital examinations, speculum stretchings with or without anesthesia, hymenectomy and even superficial midline or angle incisions were done, but the complete cure was lacking.

Fortunately with the advent of routine premarital examinations we can often diagnose

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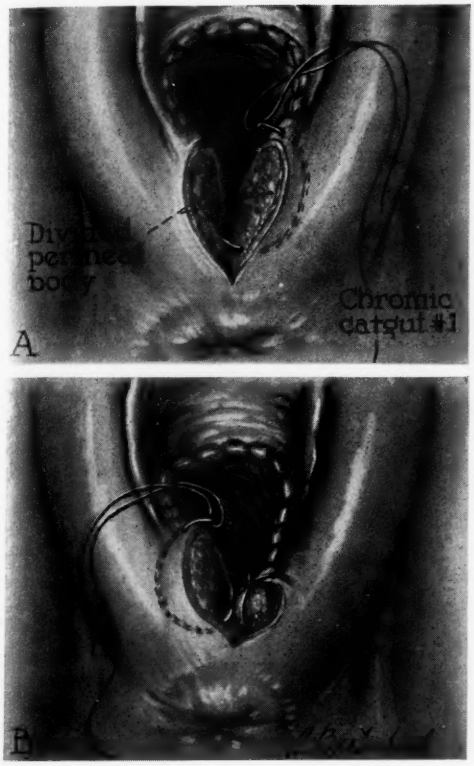

Fig. 3A. Lateral suturing of divided perineal body.
Fig. 3B. Lateral perineal body transfixed and tied.

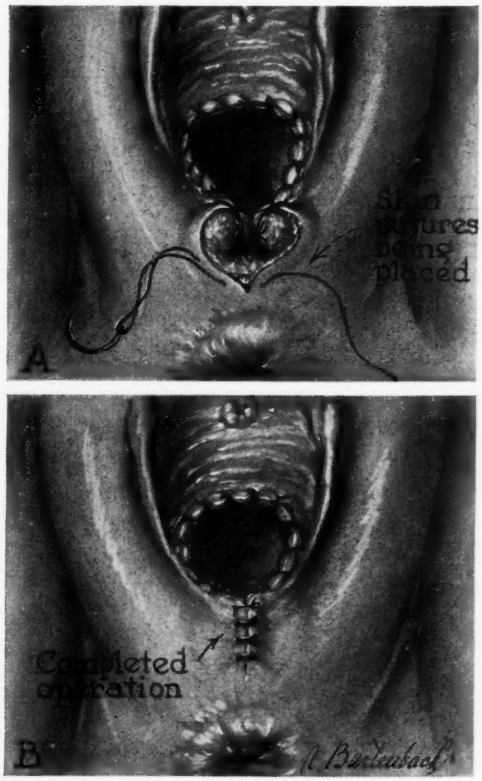

Fig. 4A. Skin sutures. Fig. 4B. Note increased size of vaginal introitus.

and prognosticate to the patient the probability of dyspareunia or complete inability at coitus. However, she is instructed to make a natural attempt at sexual congress, but if it is not fruitful, she should return for further management. We feel that by this prophylactic discussion with the patient, the far reaching psycho-trauma with the resultant anxiety and fear neuroses may be avoided, thereby preventing an unhappy married life.

It is our opinion that the management of this problem requires not only a psychiatric and immediate surgical approach, but also an after treatment which is usually not completed until a month or six weeks subsequent to the operative procedure.

We appreciate the psychosomatic potentials of this problem, and if our reassurances do not suffice, we refer her for further psychiatric therapy. This paper deals primarily with the surgical restoration to a relatively normal size entroitus of the vagina.

In our opinion the best surgical approach is: a complete circular hymenectomy, and then a midline perineotomy performed with the finger in the rectum as a guide so that the incision can be made with impunity down to the rectal sphincter without injury to this structure. The longitudinal incision is made into the central point of the perineum which is a fibromuscular tendonous mass composed of the constricting muscles of the vagina, transverse perineal muscles, and fibers of the levator ani muscles and crisscross fibers of the anal sphincter.

This longitudinal incision is now sewed transversely with fine chromic catgut and then the mucous membrane is sewed to the skin

with interrupted fine silk sutures all along the line of the hymeneal excision.

A sulfa pack is inserted into the vagina and is removed in 24 or 48 hours. The patient is permitted early ambulation and one week after surgery, when there is diminishing local edema, vaginal dilatations are started with progressive graduation and are continued twice weekly for approximately a month.

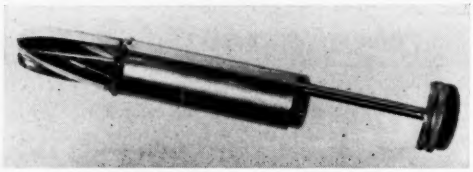

Fig. 5. Photograph of dilator with the blades closed.

Fig. 6. Photograph of dilator with large latex finger cot over the blades.

We have suggested a dilator which is more symmetrical than a speculum and seems to give a more even and circular distribution to the area which is to be dilated.

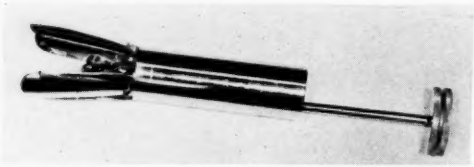

Fig. 7. Photograph of the dilator with the blades open.

A month or six weeks after the operative procedure, normal coitus can usually be enjoyed with little if any evidence of the accompanying vaginismus.

SUMMARY

The important, but often underestimated subject of the rigid hymen and perineum early in marriage, is discussed with relation to its psychiatric and surgical approach. Emphasis is placed upon the fact that with the finger in the rectum a liberal incision can be made into the perineum without injury to the rectal sphincter.

The after treatment of progressive graduated dilatations is a very integral part of the procedure. A dilator is presented which seems to give a more uniform and symmetrical dilatation. Accompanying illustrations are presented for the purpose of clarifying the subject matter.

RIASSUNTO

L'A. discute questo soggetto, non sufficientemente valutato, sotto l'aspetto psichiatrico e chirurgico. Sottolinea il fatto che con un dito introdotto nel retto un'incisione relativamente ampia puo' essere eseguita sul perineo senza danneggiare lo sfintere rettale. Segue una dilatazione progressiva con dilatatori atti a distendere piu' uniformemente e piu' simmetricamente la vagina. La procedura operativa e' illustrata da figure.

SUMARIO

El autor discute la importancia del himen rigido y del perine el los matrimonios recientes y bajo el punto de vista de su picologia y de su tratamiento quirurgico. Con el dedo en el recto el cirujano puede hacer una incision liberal del perine sin peligro de cortal los esfinceteres del ano. El tratamiento post-operatorio de dilatacion gradual y progresiva es una parte integral del tratamiento. El autor presenta un dilatador que favorece la dilatacion uniforme y simetrica. Una serie de ilustraciones se presentan para clarificar los puntos mencionados.

SOMMAIRE

Le traitement au commencement du mari- age, de l'hymen et du péroné rigide, est discut et l'auteur décrit le traitement de cet état av ses rapports pscychiatriques et chirurgicau Il dit qu'en plaçant le doigt dans le rectum on peut faire une incision généreuse du péron sans blesser le sphincter rectal. Après l'opéra tion, on aura recours à la dilatation pr gressive du rectum. Il présente un dilatateu qui obtient une dilatation uniforme et sym-

trique. L'auteur présente des illustrations, démontrant les indications et les méthodes qu'il emploie.

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Rational Principles of Early Ambulation

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TEN years ago early ambulation was considered a "crack-pot" idea. Today, it is recognized and is rapidly approaching a "must" procedure following a surgical operation. Recognition rests on rapid recovery from the surgical ordeal. However, early ambulation has encountered the same difficulties that hindered acceptance of sterile technique over fifty years ago. Those who practice this procedure wholeheartedly and to the fullest extent now consider early ambulation indispensable to the well-being and safety of the surgical patient. From my experience and the experience of others, it has been found to save lives by hastening recovery, thereby preventing many fatal complications. It acts by rapidly restoring normal function of vital organs which have become crippled by surgical trauma.

Today, the procedure, as carried out in this country, varies considerably with different surgeons. Some surgeons get patients out of bed the day after operation; others on the second, third, fourth, and even the fifth postoperative day, and call it early ambulation. Then, there are surgeons who allow patients out of bed only when they have undergone the less serious surgical procedures; while with patients who have undergone the more serious procedures, they "wait and see" how the patients get along and, when "all is well," get them up but restrict their activity. Still others only permit their patients to sit in a chair when out of bed. These various ineffectual methods of management are responsible for the lack of uniformity of results as reported in the literature, particularly as to its value in postoperative phlebothrombosis and consequent pulmonary embolism.

When should patients be subjected to ambulation after operation, and what should be the procedure after the first out-of-bed period? What types of incisions and suture materials insure security of the wound in patients subjected to early ambulation? The answers to these questions are understandable only when considered from a physiologic and an anatomical viewpoint.[1]

We all appreciate the fact that the normal involuntary functions of the body are controlled and regulated chiefly by reflex action through the involuntary nervous system which consists of two divisions, the sympathetic and the parasympathetic. Generally speaking, these two divisions oppose each other; the one activates, and the other inhibits the functions of glands and involuntary muscles to meet shifting body requirements.

There are diseases that appear to be related to a long period of imbalance between the sympathetics and parasympathetics, such as peptic ulcer and essential hypertension. Vagus section is a recommended treatment for the former, and sympathectomy for the latter. A similar imbalance, though more severe, takes place after a major surgical operation. The surgical trauma initiates a complex series of nerve impulses of such magnitude and intensity that glands and involuntary muscles are activated or inhibited to an abnormal degree with consequent abnormal function. The abnormal function thus induced interferes with body secretions, the normal flow of body fluids, the required intake of oxygen, and the elimination of waste.

The functional disruption of otherwise normal organs as a result of the removal of a diseased structure is usually so pronounced that the patient is more ill during the immediate postoperative period and for several days thereafter than before the diseased organ was removed, even though the requisites for normal body function have not been altered. Thus, the initial illness after an operation is functional or neurogenic in character, in contradistinction to an organic illness. The more severe the functional illness after operation and the longer it is permitted to continue, the greater will be the danger of development of postoperative complications.

Prolonged abnormal function of this char-

acter in the presence of cytolytic toxins from trauma, which soon accompany the functional changes, is responsible for a vast majority of the most serious postoperative complications, particularly those related to respiration, circulation, and digestion.

Now let us consider how trauma, through reflex action, produces abnormal function in these three systems, and how normal activity may be rapidly restored by means of early ambulation.

RESPIRATORY SYSTEM

Surgical trauma, especially after an abdominal operation, arouses nerve impulses of such magnitude that there is an overflow of these impulses into the inhibitory fibers of the phrenic nerve. These inhibitory impulses diminish the tone and contraction of the diaphragm. The diaphragm becomes relaxed, occupying a high position in the chest, and its excursion is limited, while other respiratory muscles are usually in reflex spasm. Thus, the expansion and contraction of the thoracic cage is diminished, reducing tidal air and vital capacity. The reduction of vital capacity is most pronounced after upper abdominal operations. In some instances, according to Churchill and McNeil,[2] the reduction may be as much as 80 percent, and two weeks are usually required for the vital capacity to return to normal (Fig. 1). Their patients were confined to bed.

The limited excursion of the thoracic cage, owing to this reflex inhibition, is compensated by rapid, shallow breathing; and, according to Haldane, Meakins and Priestly,[3] rapid, shallow breathing causes anoxemia. Therefore, this reflex limits oxygen supply, eventually causing adverse changes in the composition

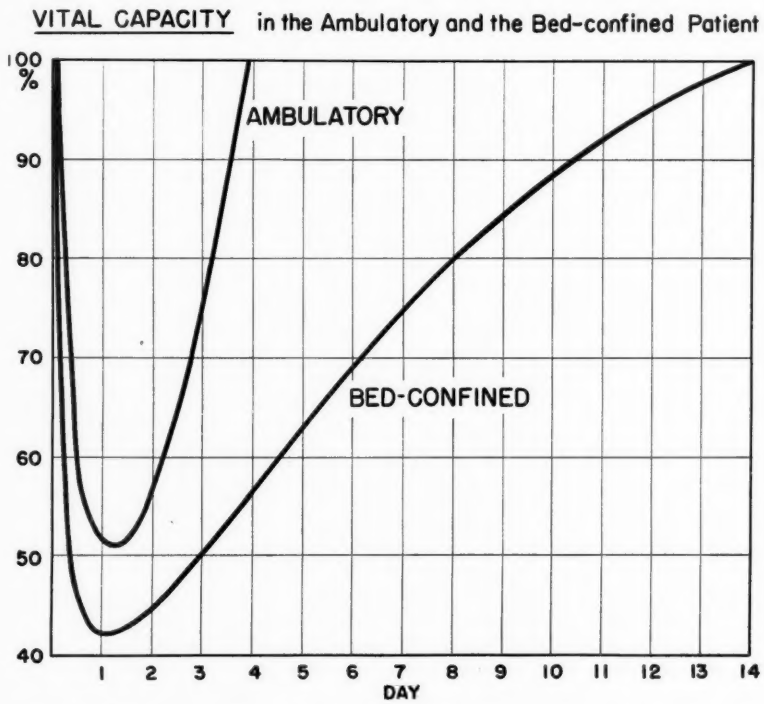

Fig. 1. Effect of laparotomy on vital capacity in the bed-confined and the ambulatory patient. (Medical Physics—in the hands of the publisher.[3])

of the blood itself. There is another adverse factor from inhibition of the diaphragm after operation. The limited excursion of the thoracic cage limits the contraction and expansion of the bronchioles; these movements are synchronized. The restricted expansion of the bronchioles in the presence of excess mucus from the activated bronchial glands is favorable to the development of bronchial obstruction; and, according to Hilding,[4] as the mucous plugs are removed by ciliary action, a negative pressure develops in the air cells (Fig. 2). If this process becomes extensive, it may cause collapse of an entire lobe. This seems to be the basic principle in the development of postoperative pulmonary atelectasis.

How can this reduction in chest expansion and contraction after operation be overcome, and how can the ill effects of excess mucus be eliminated during this critical period?

The reflex inhibition of chest expansion and contraction is most pronounced immediately after operation; it is then that the vital capacity is at its lowest ebb (Fig. 1). Therefore, an effort should be made at this time to overcome the abnormal function of the diaphragm —not one, two, three, or four days later when complications have already developed. How can this be done? By the upright position, coughing, and walking. The pull of gravity upon the abdominal contents lowers the diaphragm when in the upright position, and thereby increases vital capacity. Coughing expels mucous plugs, while walking stimulates deep breathing. Using this procedure, the vital capacity after an abdominal operation returns to normal in two to five days[1] (Fig. 1), instead of in fourteen days as usually required by bed-confined patients.

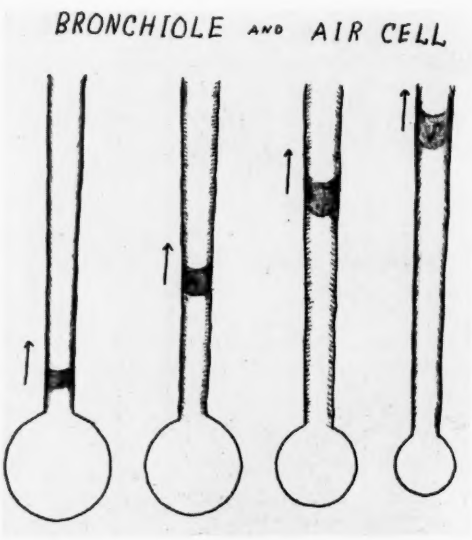

Fig. 2. Diagram representing the removal of mucous plugs in a bronchiole by ciliary action, causing negative pressure in the air cell, and collapse. As the mucous plugs converge to the larger bronchi, their removal may cause atelectasis of an entire lobe of the lung (as described by Hilding).

In 1930, Patey[6] commented: "Many efforts have been made by surgeons to overcome this inhibition of the diaphragm after an abdominal operation, but so far without any uniformity of success. Postoperative deep breathing exercises have little effect. . . . We must therefore conclude that at present the problem of efficient diaphragmatic movement in the presence of an abdominal wound remains unsolved." His patients were confined to bed.

Those of you who practice "early" ambulation have the solution to this problem, and appreciate that walking at regular intervals after operation is imperative for rapid recovery.

CIRCULATORY SYSTEM

Reflex action after surgical intervention also initiates abnormal function of the circulatory system. In the area of trauma there is vasodilatation, a reaction of inflammation, and remote from the area of trauma there is a compensatory reflex vasoconstriction. Fear and pain may also contribute to vasoconstriction. These changes tend to retard the flow and distribution of blood. Then, cytolytic toxins soon bring about changes in the blood itself: there is an increase in sedimentation rate, in leukocytes, and in fibrinogen.

Knisley, Bloch, Eliot and Warner,[7] by means of a specially constructed microscope, have observed that surgical trauma produces a sludge consisting of red and white cells in the blood stream (Fig. 3).

The red cells, which normally repel each other, become covered with a sticky protein substance that causes them to become agglu-

nated in masses. These masses resist passage through the arterioles, and frequently cause complete obstruction in the flow of blood. The endothelium of capillaries and small veins is then deprived of oxygen and becomes increasingly permeable, consequently plasma is lost excessively.

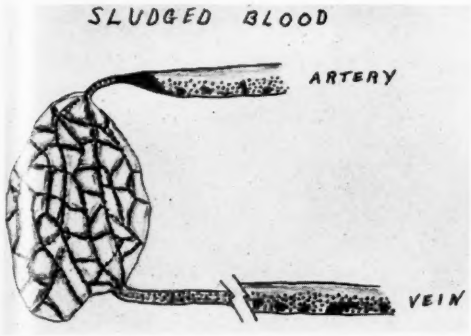

Fig. 3. Diagram of sludged blood obstructing the arteriole; also sludge attached to the wall of the vein (as described by Knisley, Bloch, Eliot and Warner).

If this condition becomes widespread, shock may develop. In addition, in the horizontal position or where the blood is flowing slightly uphill (as in the case of a patient in bed with the head elevated), the sludge has a tendency to settle to the bottom of the vessel and flows slowly as compared to the clear supernatant plasma. The slowly-moving, sticky sludge may come to a standstill and "become cemented together in long gelatinous masses." Should the sticky mass become attached to the vessel, it may form the nidus for the development of a large thrombus. Thus, the work of Knisley and his coworkers provides a plausible answer to the question of the etiology of postoperative thrombo-embolic disease in the bed-confined patient.

With this understanding of the changes in the blood after operation in the presence of vasoconstriction, the necessity for muscular activity, particularly walking, is immediately understood. Walking opens the arterioles, and the volume of blood is markedly increased; this permits the sludge to pass, and materially hastens the return flow of blood in the veins. Since thrombo-embolic disease is usually associated with the deep veins of the legs, we have taken another precaution to avoid sludge becoming attached to these vessels during the in-bed period. This is done by means of an exercise chart which is placed in constant view of the patient (Fig. 4).

The acceleration in the flow of blood as a result of these exercises and walking is a means of preventing the formation of a clot or of dislodging a small, loosely attached mass before a massive fatal clot can form. Neither heparin nor dicumarol has been required or employed in my practice since the institution of early ambulation in 1938, in a series of over 2,500 abdominal and many other opera-

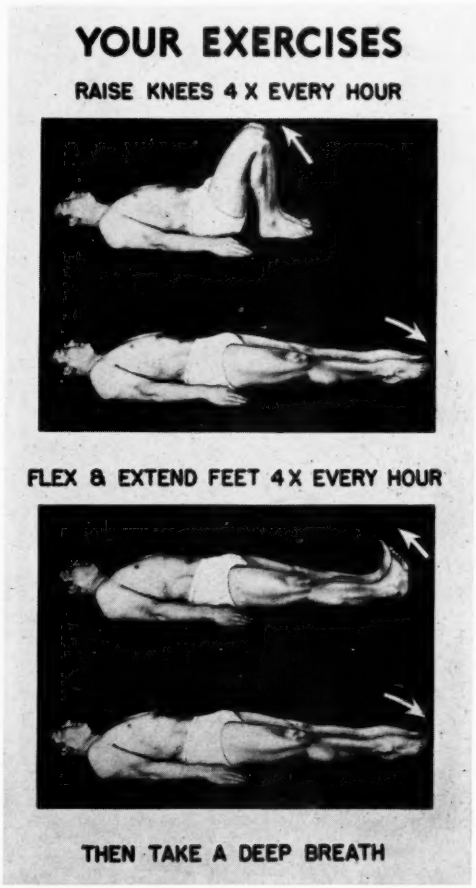

Fig. 4. Chart placed in patients' rooms to demonstrate in-bed exercise (Leithauser[1]).

tions. Not a single pulmonary embolism has occurred, nor has there been a recognizable phlebothrombosis in the deep veins of the legs. These results, in the presence of the reported high incidence of thrombotic disease, are sufficient evidence of the inestimable value of in-bed leg exercises and early ambulation in combating this most serious postoperative complication.

DIGESTIVE SYSTEM

Reflex intestinal inhibition after operation requires very little comment. Nerve impulses from trauma, fear, and pain are usually of such intensity that there is an overflow into the sympathetic nervous system which is inhibitory to the intestinal musculature. This overflow probably occurs to some degree after every abdominal operation. The extreme state of intestinal inhibition is recognized as adynamic ileus. Distention, when associated with nausea and vomiting, is indeed distressing; however, the more harmful effects probably come from pressure on the already crippled diaphragm and on the deep veins in the abdomen, which further embarrasses respiration and circulation. Exercise, especially walking, will also improve this reflex inhibition, promoting appetite and bowel evacuation by increasing the tone and motility of the intestinal tract. Ambulatory patients rarely require enemas.

INCISIONS

It has been a traditional concept that the security of abdominal incisions is incompatible with ambulation after operation. There is justification for this belief. The natural presumption is that the strain from ambulation would greatly increase the incidence of disruption and postoperative hernia. Reports in the literature reveal that approximately one celiotomy wound of every hundred disrupts. According to Sloan,[8] the longer the vertical incision, the weaker the incision line will become, and in ten years, 80 percent of incisions (vertical rectus) over five inches long show evidence of herniation or weakness.

However, paradoxical as it may seem, the recent literature on early ambulation reveals that the incidence of disruption and postoperative hernia is decreased in the ambulatory patient. This reduction, without question, is attributable to the fact that surgeons have acquired greater respect for muscle function, influencing their choice of the type of incision and suture material for patients whom they consider candidates for early ambulation.

In a consecutive series of over 2,500 celiotomies by the author, in which the patients were subjected to early ambulation after abdominal operation, there has not been a disruption, and only three incisional hernias have occurred. These results are attributed to the proper selection of incisions and suture materials (Fig. 5).

Abdominal incisions in these patients have been made in such a way as to retain the integrity of the fibers of the transversalis muscle. Only muscle-splitting, transverse, or midline incisions were employed. There is no strain on the sutured layers of the muscle-splitting incision. This incision was closed, in this series, with single 000 chromic catgut. In the transverse incision, there is no strain on the sutured layer of the transversalis muscle and its aponeurotic fibers. Contraction of these fibers actually compresses the incisional gap. This layer of the transverse incision was closed, in this series, with double 000 chromic catgut. However, in the transverse incision, the fibers of the external oblique muscle and its aponeurotic fibers are cut at right angles, therefore separate on contraction of this muscle. Interrupted sutures of alloy steel wire were used in this layer. In the midline incision, there is considerable pull on the suture line; however, the fascial layers are fused in the midline, and therefore hold sutures well. This layer was closed, in this series, with double loop sutures of alloy steel wire. The above incisions when closed in this manner need give no fear of disruption or postoperative hernia.

CONCLUSIONS

Early ambulation does not increase the danger of wound disruption or postoperative hernia provided the integrity of the fibers of the transversalis muscle are preserved, and proper suture materials are used.

The patient who is more ill derives a greater benefit from early ambulation than the patient who is less ill. The reason is obvious. Early ambulation promotes the normal function of

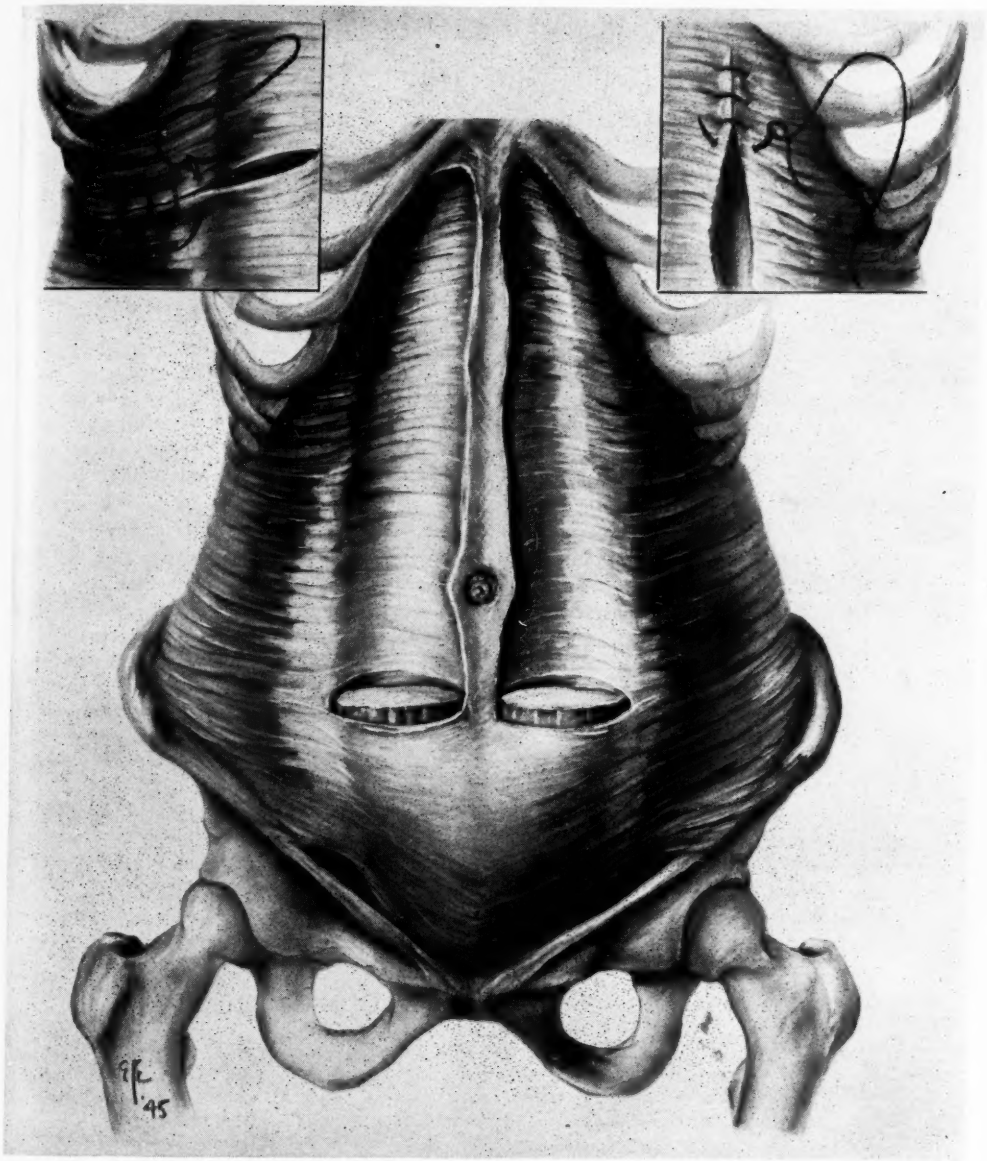

Fig. 5. Transversalis muscle exposed by removal of all structures anterior to it. Note the transverse direction of its fibers. Inset, upper left, shows how firmly the sutures grasp the fibers in the transverse incision. Inset, upper right, shows contrasting difficulty of attempting to suture the cut ends of the fibers in the vertical rectus incision (Leithauser[1]).

vital organs; lessens the severity of the illness after operation; improves the appetite; prevents postoperative atelectasis and pneumonia; prevents thrombosis and embolism; practically eliminates the need for the bed pan; shortens the period of convalescence by approximately one-half; and greatly reduces hospital expenses.

RIASSUNTO

Una precoce deambulazione non accresce il pericolo di una discissione delle ferite o di un'ernia postoperativa, purche' le suture siano state eseguite con materiale adatto e le fibre dei muscoli trasversali siano state rispettate. Da una precoce deambulazione beneficiano maggiormente i pazienti piu' gravemente malati e cio' per molteplici ragioni: perche' questa promuove una normale funzione negli organi vitali; diminuisce la gravita' della malattia dopo l'operazione; aumenta l'appetito; previene un' atelectasia ed una polmonite postoperatoria, nonche' trombosi ed embolismi; perche' elimina praticamente la necessita' della cosidetta padella; perche' abbrevia di circa meta' il periodo di convalescenza e riduce quindi corrispondentemente le spess di ospedalizzazione.

SUMARIO

La ambulacion temprana no aumenta el peligro de dehiscencia de la herida ni favorece la hernia post-operatoria siempre y cuando se hayan preservado la integridad de las fibras del musculo transverso abdominal y se haya usado un material de sutura apropiado. La ambulacion temprana favorece mas al paciente que esta mas enfermo, por cuanto estimula el funcionamiento normal de los organos vitales, incrementa el apetito y previene la atelectasia post-operatoria y pulmonia; previene la trombosis y el embolismo; elimina casi practicamente el uso del basinete; acorta el periodo de la convalescencia en la mitad; y, finalmente, reduce considerablemente los gastos hospitalarios.

SOMMAIRE

L'ambulation précoce n'augmente pas le danger de disruption de la plaie ou d'une hernie postopérative, pourvu que l'integrité des fibres du muscle transversé soit préservé et qu'on ait employé un matériel de suture approprié. L'opéré qui est plus malade, présente un plus grand bénéfice de l'ambulation précoce, que le malade qui est moins malade. L'ambulation précoce favorise la fonction des organes vitaux, diminue la sévérité des malaises postopératoires, augmente l'appétit empêche l'atélectase et la pneumonie postopératoires, empêche le thrombose et l'embolisme, élimine l'emploi du bassin, abrège la période de convalescence et diminue pour le malade les dépenses de son séjour à l'hopital.

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Plastic Repair of the Female Breast

Physical and Psychic Indications Plus Author's Technic

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PLASTIC surgery in general, and that of the breast in particular, have been subjected to severe criticism, largely because the term has been used by quacks, charlatans and some unscrupulous surgeons to apply to the practices which disgrace the surgical art. So-called plastic surgery of the face as well as of the breast has been offered to the credulous and foolish with the promise of changing ugliness to beauty. Not infrequently the victims have been left deformed and more repugnant than they have been. Nevertheless, true plastic surgery is a legitimate surgical art. Its object is the removal or masking of a repugnant disability or deformity.[12]

The function of the female breast in reproduction readily explains its appeal to the human imagination. The breast idealized by artists is a thoroughly normal one—a hemispheric body with the nipple projecting from its center, resting on the wall of the chest on either side of the sternum and extending from the level of the second to the sixth rib and from the sternum to the axillary border. The outline of the base is elliptic, 10 or 12 cm. across and about 1 cm. less in height, projecting about 5.5 cm.

In young women who have not been pregnant, the amount of glandular tissue is small in comparison with the fat between the lobules. The gland is supported by enveloping skin and the superficial fascia of the thorax, which invests it and gives off septa (Cooper's suspensory ligament). It also penetrates the gland and helps toward its support. A layer of fat separates the gland from the underlying pectoralis major muscles.

In hypertrophy due to pregnancy, obesity or congenital tendency, the weight of the breast strains the suspensory tissues. Marked discomfort as well as unsightliness result from stretching of the skin and ptosis.

Knowledge of the vascular supply of the breast is important to successful surgical treatment. The lateral portion of the gland is supplied by the long thoracic artery, a branch of the axillary. Since that portion of the gland deriving its arterial and venous network from this source is in our methods always separated from its basis and sometimes resected, the vessels supplying the central portion of the gland and the nipple must be preserved, principally the second, third and fourth perforating branches of the internal mammary artery.

Of the three main constitutional types of deformity of the breast, *true hypertrophy*, with a marked increase in glandular tissue without a corresponding oversupply of fat, is rare. This type appears immediately after the onset of menstruation and is completely developed in a few months. The breasts may reach enormous proportions, with unbearable weight impeding normal activity.

Hypertrophy with fatty degeneration is common. In this type, fatty, not glandular, tissue is excessive. Sometimes the breasts extend to the navel. This deformity is as common in young girls as in older women, and often it is in striking contrast to the shapeliness of the rest of the form. It inflicts profound psychic as well as physical discomfort. The dragging sensation at the shoulders and chest is not relieved by change of position. Faulty posture results, detracting further from the woman's appearance. Circulatory disturbance in the engorged part may cause eczema, with itching to add to the patient's distress.

Atrophy may involve the gland or the subcutaneous fat or both. Usually it is a stigma of aging, but it is growing more common in young women, owing to the mania for slimness.

INDICATIONS FOR RECONSTRUCTIVE SURGERY

The plastic reconstructive operation with elevation of the re-formed organ is indicated by symptoms the patient complains of and the experience of the surgeon.[9] Both physical and mental complaints must be considered.

Pain (mastodynia) and circulatory disturb-

ances are the important physical symptoms. Often the latter affects the heart, with increasing discomfort, disability, debility, tumor formation and sometimes gangrene. Activities are restricted. Kyphosis, scolosis, abdominal relaxation and pulmonary and psychogastric disturbances may result. Sometimes patients restrict their diet in the hope of correcting the condition, and nutritional deficiency follows. Hormonal disturbances have been observed to result from hypertrophy of the breasts, and correction may be followed by improvement in ovarian function. The liability to cancer, sarcoma and Paget's disease is reduced by surgical correction.[3]

Mental complaints make the case even stronger. Women with heavy, sagging breasts are keenly aware of the handicap to their appearance. Many social activities are closed to them, and they are under a vocational disability, not only because good appearance is vital to the woman in business, but because active movement is prevented. Walking, dancing and sports are impossible. Excessive perspiration restricts a woman's social acceptance. Many women avoid social contacts and become depressed and morose, and sometimes suicidal tendencies develop.

CONTRAINDICATIONS

Pulmonary, cardiac, renal and metabolic disease are the principal contraindications to mammoplasty. Eczema, suppurative processes and scarred skin from burns must be treated preoperatively. The patient should not be operated on three days before to three days after the menstrual period. It is inadvisable to perform this operation on extremely nervous, unbalanced persons. Moreover, the experienced surgeon should not refuse to perform the operation without good reason, for by so doing he may leave the patient to the unscrupulous and the inexperienced, with unpleasant and sometimes disastrous results.[11]

TECHNIC

The proper technic must aim to achieve the following general points:

1. The operation must be free from danger.
2. It must not leave behind unsightly scars.
3. The function and blood supply of the gland structure must be respected.
4. There must be a certain grade of permanency regarding the result.

Besides these general precautions regarding the result of mammoplasty, our technic was developed to achieve:

1. Shapely breasts of firm consistency and virginal appearance.
2. Nipples with their areolas of circular design protruding at the highest point of the breasts.
3. Symmetric divergence of the axes of the breasts.

Besides those features just stated the skin itself for the new breast must be firm. This is achieved only by using the skin above the level of the nipple in the reconstruction of the breast. The lateral prominence of the hemispheric breast must be harmonious as it is in nature, i.e. without formation of the skin pouches at this part.

The scars must be confined to the circumareolar area and the submammary fold. All vertical scars are esthetically contraindicated and practically always conspicuous. The nipple must be entirely visible in profile, and from the front view must be placed symmetrically with the other nipple, both in relation to the sternal line and in height. Any convergent strabismus of the nipples must be avoided.

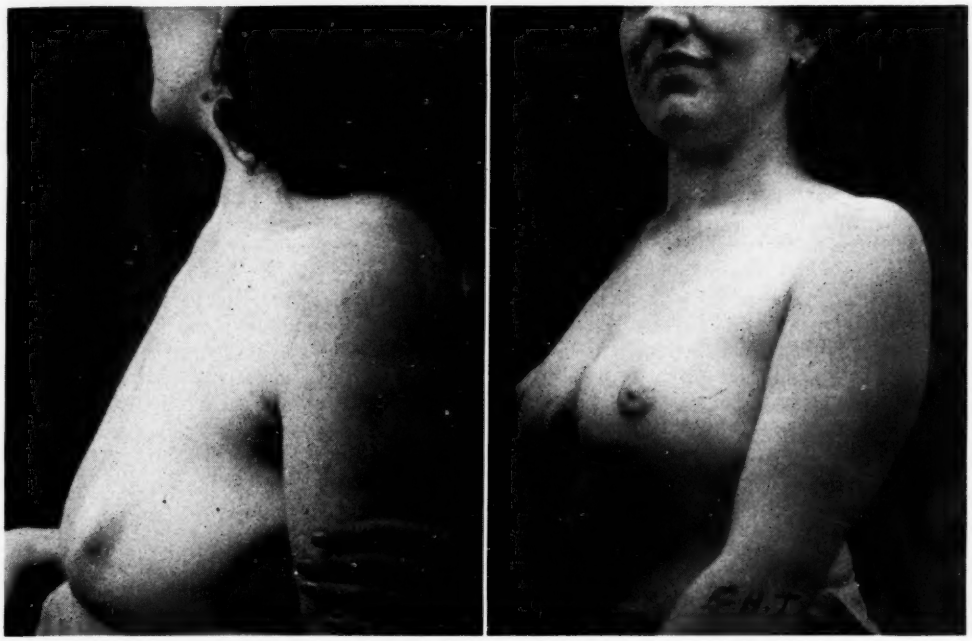
HIGHLIGHTS OF OUR TECHNIC

With the circumareolar skin evenly stretched by the assistant's hands, the mammilla and the areola are circumcised with a 1.5 cm. of de-epithelized cutis left all around.

A slightly sinusoid incision above the circumcised areola and an incision laid parallel to the submammary fold about 1 cm. above, the two meeting laterally in the outer axillary line, medially about 2 cm. from the lateral sternal line leaving a crescent-shaped area of skin between them to be excised.

The skin including a fairly thick pad of subcutaneous fat above the entire upper part of the gland is undermined until one reaches the proximal margins of the gland where it is only loosely attached to the pectoral fascia. Thus the greatest part of the breast is denuded.

Nearly three fourths of the denuded gland are now—mostly bluntly—separated from the



Before After

pectoral muscle respectively the fascia. The gland is elevated in its two lateral quadrants, shutting off the blood flow from the long thoracic artery. It is separated also in the proximal part of the upper inner quadrant and slightly in the lower inner quadrant, where the small perforating arteries and veins are divided.

The remaining gland-flap is supplied entirely by the three branches of the internal mammary artery, which are enclosed in the pedicle of the flap.

In the hypertrophic breast, nearly the whole upper half of the gland-fat flap is resected with an amputation knife, which is carried from the surface vertically through the whole thickness of the gland down to the pectoral muscle. Depending on the size of the gland, the part lateral to the nipple and part of the lower portion also may be resected. The reduced, properly trimmed fat-gland flap then is molded into a snail-like, conic shape by clockwise rotation of its peripheral free end which includes the nipple. The spirals are loosely but carefully joined with catgut stitches, without strangulating the fat tissue to avoid necrosis of it. The whole cone is fastened to the pectoral muscle with a few penetrating stitches in the lateral and upper portions.

After fenestration of the skin flap, which is going to envelop the resected breasts contents, and buttonholing of the nipple and its areola into the opening, the skin flap is attached to the cone with catgut stitches from inside with great care being taken not to perforate the skin surface. This procedure eliminates empty spaces between skin flap and cone and avoids accumulation of blood and lymph between them. Later on the ugliness of pouches in the lateral part of the new breast is by this technical feature obviated. After this has been accomplished the superfluous parts of the skin flap in the lateral regions are removed to avoid the unsightly bulges seen so often after mammoplasty. With fine silk, the buttonhole wound margin is sutured to the transposed nipple and areola. With heavier

silk or cotton, the horizontal submammary incision margin is fastened to the lower margin of the skin flap. A drain is inserted into the lateral corner of the lower suture line of each breast, and left for 24 hours.

The technic for atrophic, saclike deformity of the breast is approximately the same, except that little or no fatty and glandular tissue is removed.

After three months, aftercorrection can be done, usually with the patient under local anesthesia. Shrinkage of fatty tissue, the blood supply of which was partially interfered with at the first operation will be complete at this time, and the amount of excess skin above the diminished fat can be seen distinctly. The redundancy is corrected together with other incongruities which could not have been avoided at the earlier operation. The horizontal scars are excised, and the wound margins reunited in new suture lines corresponding exactly with the submammary folds.

SUMMARY

The described method has been developed to minimize risk completely, preserve the function and blood supply of the gland structure, and achieve shapely, firm breasts diverging symmetrically and without unsightly scars. It is applicable in approximately 90 percent of all breast hypertrophiies of both dystrophic and adiposohypertrophic types. The gross initial operation is performed in one stage under light general anesthesia. The aftercorrections, leading to the final shapeliness, can be performed under local anesthesia. The main feature of our technic is the formation of a fat gland flap with mesial pediele of an adequate blood supply to the nipple and the areola. Technic was developed during the years 1935 to 1937 and was first described at the Second European Congress of Structive Surgery at the Royal College of Surgeons, London, 1937. Its basic features have been adopted by Gillies and McIndoe in their method published in 1939.

RIASSUNTO

Il metodo descritto dall'A. e' rivolto a ridurre ad un minimo il rischio operatorio, a conservare la vascolarizzazione e la funzione della ghiandola, ad ottenere delle mammelle ben conformate e divergenti simmetricamente, senza cicatrici deformanti. Puo' essere adottato nel 90 percento dei casi di ipertrofia mammaria, sia del tipo distrofico, sia del tipo adiposo—ipertrofico. L'operazi one principale viene eseguita in un solo tempo, sotto lieve anestesia generale: le correzioni successive, atte a perfezionare il risultato estetico definitivo, vengono invece compiute in anestesia locale.

La principale caratteristica del metodo consiste nella formazione di un lembo adiposo—ghiandolare, con un peduncolo prossimale atto a supplire una sufficiente quantita' di sangue al capezzolo ed all'areola.

La tecnica operatoria, sviluppata nel 1935-1937, e' stata descritta per la prima volta nel 1937 al secondo Congresso Europeo di Chirurgia plastica presso il Regio Collegio di Chirurgia di Londra. Le caratteristiche principali dell'operazione sono state adottate nel metodo pubblicato da Gillies e McIndoe nel 1939.

SUMARIO

Se ha desarroyado un metodo operatorio de la glandula mammaria que preserva su circulacion y por lo tanto su funcion, y que al mismo tiempo asegura una forma firme y estetica de la glandula, sin cicatrices muy visibles. Esta operacion es aplicable al 90% de los casos de hipertrofia de la glandula, tanto en los tipos distroficos como en los adiposohipertroficos. La operacion primaria inicial se practica en una etapa, bajo la anestesia general; las operaciones sucesivas se practican bajo la anestesia local. La caracteristicas principales de esta tecnica es la formacion de una flapa cuyo pediculo tenga una circulacion abundante. Esta tecnica se desarroyo en los anos 1935-1937 y fue presentada ante el segundo Congreso de Cirujia Estructiva del Colegio Real de Cirujanos de Londres en el ano 1937. Las caracteristicas basicas de esta operacion han sido adaptadas al metodo del Gillies y McIndos y que fue publicado por estos autores en el ano 1939.

SOMMAIRE

La méthode que l'auteur décrit a été développée afin de diminuer complètement le risque opératoire, de conserver la fonction et

la vascularisation de la glande mammaire et d'obtenir des seins fermes, gracieux avec séparation symétrique et ne laissant aucune cicatrice disgracieuse. L'opération est applicable dans approximativement 90 percentum de toutes les hypertrophies mammaires dystrophiques et adiposohypertrophiques. L'opération initiale principale se fait sous anesthesie générale légère. Les corrections consécutives ayant pour but l'embellissement, se font sous anesthésie locale. Le trait principal de la technique est la formation d'un lambeau de la glande et du tissu adipeux ayant un pédecule fournissant une suffisance de sang au mammelon et à l'aréole. La technique fut développée durant les années 1935 à 1937 et fut décrite la première fois au Second Congrès Européen de Chirurgie Plastique tenu au Collège Royal de Chirurgiens à Londres en 1937. Ses bases fondamentales furent étudiées par Gillies et McIndoe et publiées en 1939.

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Case Report

Ventral Hernia as a Complication of Pregnancy

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VENTRAL hernia during or antecedent to the pregnant state is sometimes encountered, and there are cases of hernia in which the uterus lies outside the abdomen in a hernial sac.[6] The greater number of modern textbooks are silent on the subject of ventral hernia as a complicating factor in maternity. This is surprising since the surgery of obstetrics has made great progress in late years. For many reasons it is important to determine what influence pregnancy has on this disease as a whole, whether it causes it, aggravates it, or is complicated by it.

In March, 1889, Samuel Adams[1] of Washington, D. C., reviewed the literature and found that eight cases of "Hysterocele Ventralis" had been reported and he proceeded to give a summary of each. The cases were treated in methods which varied from permitting the patient to go into labor normally, to delivery by cesarean section. Sylvester Saxtroph,[7] a Dutch practitioner in the early part of the nineteenth century, was one of the first to observe a hernia complicating pregnancy in a peasant woman who had had four normal labors. In her fifth pregnancy, the gravid uterus escaped through the abdominal wall and hung down below the knees. The case was seen by several of the most noted physicians in Holland, but none ventured to interfere. She went on to term and into labor.

Saxtroph reports that the uterine contractions forced the fetus into the abdominal cavity and through the birth canal. The reported results seem to indicate that conservative treatment was most advisable at that time since abdominal surgery was attended by far greater complications than we find today.

Levy[9] of the Touro Infirmary, New Orleans, reported a case of pregnancy associated with a marked diastasis of the recti muscles in a woman pregnant for the 13th time. One month before term, the gravid uterus has escaped into the hernial sac. At term, guarded attempts were made to return the uterus to the abdomen and to force the presenting part into the pelvis. This was unsuccessful. He then performed a Porro-cesarean section with repair of the hernia. His patient made a relatively uneventful recovery, but he failed to state the indications for the removal of the uterus.

Rongy[8] in 1922 reported a case of a woman who had a marked median ventral hernia through which protruded a gravid uterus, covered only by the skin and subcutaneous fat of the abdominal wall. This woman had had four previous cesarean sections. He performed the fifth cesarean section and then repaired the hernia. Boys[2] reported a case which he considered a strangulated hernia containing a pregnant uterus. He performed a classical cesarean section and delivered a 10 pound, 14 ounce female infant. Neither the uterus nor the adnexae were found to be gangrenous and apparently were not strangulated. In an exhaustive review of the literature, he found that only eight cases of hysterocele with strangulation have been reported.

CASE REPORT

Mrs. L. B., a 35 year old multipara, was admitted to the hospital, Jan. 7, 1947 complaining of severe back pain, low abdominal pain and occasional nausea and vomiting. The patient was in her ninth month of gestation and the following history was obtained:

During childhood, the patient had measles, age six; pertussis, age eight; and bronchopneumonia, age 17. At the age of 20 she had an appendectomy. Her menses started at the age of 14, and were regularly 28 days apart, lasting three days with moderate flow and slight dysmenorrhea. She was married in 1937.

The patient's first pregnancy was in 1941 and resulted in cesarean section. During that preg-

nancy she gained over 30 pounds and during the last trimester she complained of prepubic, sacral, and ankle edema. She also had three episodes of hyperemesis gravidarum. Her B.P. at term was 100/70, pulse 72, RBC 2,900,000, hemoglobin 60 percent, and WBC 12,000. The patient went into labor 29 days after the date of expectancy. After 16 hours of labor, a roentgenogram revealed the fetus lying in the transverse position with the right shoulder presenting. A low-flap cesarean section was performed and a normal, living, female infant was delivered weighing 10 pounds, 12 ounces. Her postoperative course was uneventful.

In May, 1946, the patient conceived again and suffered from intermittent episodes of abdominal and low back pain with constipation which lasted throughout her pregnancy. Her weight which was usually 160 pounds was 205 pounds upon admission to the hospital. Her blood pressure during two prenatal visits was 120/80 and 116/80, hemoglobin was 76 percent, RBC 4,000,000, and her urine showed a trace of albumin on both visits. She stated that during the first few months of pregnancy she had worn a corset, but had discarded it when she discovered that it increased her nausea and vomiting and her abdominal pressure and shortness of breath. In the month prior to admission, she had noticed a red, excoriated area on the most dependent portion of the abdomen.

Physical examination revealed an obese white female, age 34, lying comfortably in bed, and complaining of abdominal pain. Her head and eyes

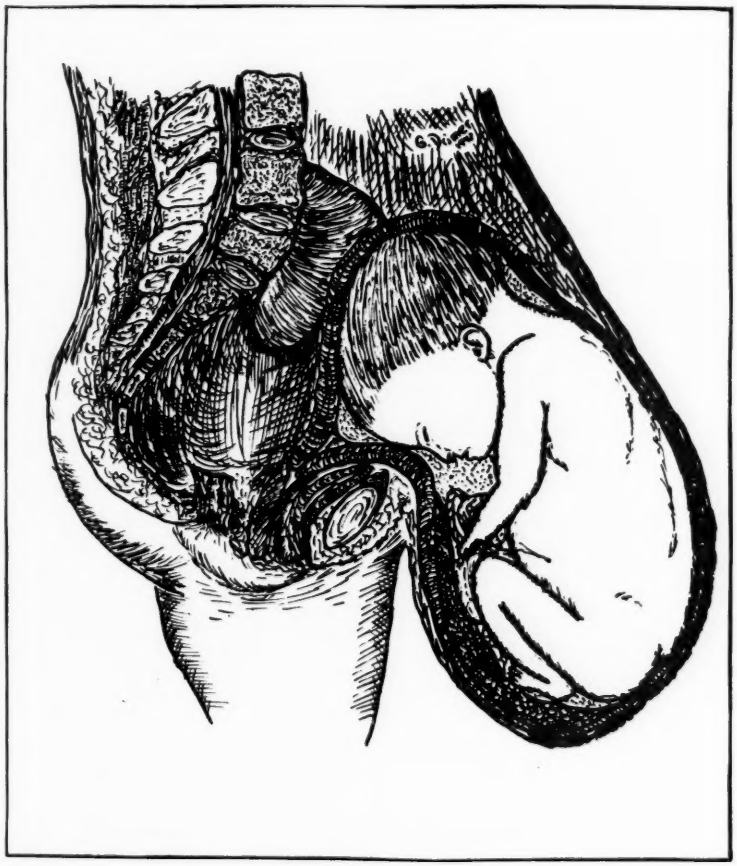

Fig. 1. Sagittal section reconstructing pelvic relationships with fetus lying within the uterus in the hernial sac.

were normal, and the ears, nose, and throat were negative. Examination of the neck revealed the trachea in the midline, thyroid not enlarged, and no palpable lymph glands; chest—no masses in the breasts, lungs clear and resonant; heart—sounds of good quality, no murmurs audible, blood pressure 120/80, pulse 82 and regular; abdomen—obese, pendulous, hanging between the thighs.

There was an irregular, elliptical area of excoriation approximately three inches long and one inch wide at the most dependent portion of the abdominal wall. A midline suprapubic scar from the previous cesarean section was found to be stretched in all directions. There seemed to be little or no tissue between the skin and the underlying uterus. A right pararectus appendectomy scar was also found to be stretched and distorted. The fetal parts were easily palpable through the paperthin tissue covering the uterus. The fetal head was found above the pelvic brim with occiput to the left, the small parts to the right and the breech in the most dependent portion of the uterus (Fig. 1). Extremities—reflexes normal, two plus pitting edema of both ankles.

Roentgenographic examination revealed a full term fetus lying completely outside the pelvis (Fig. 2). There was no cephalopelvic disproportion.

Laboratory Data: Blood count—RBC, 3,850,000, hemoglobin 76 percent (Sahli), WBC 7,700, polys 78 percent, lymphs 12 percent, monos 7 percent; eosins 3 percent. Blood chemistry—sugar 89 mgs. percent, urea nitrogen 16.4 mgs. percent, creatinine 1.2 mgs. percent. Urinalysis—(voided specimen) specific gravity 1.020, albumin two plus, sugar, acetone, diacetic acid and bile absent. WBC 6-8 per h.p.f., RBC 25-30 per h.p.f., few epithelial cells, no casts. Blood Type—Type A, Rh positive, Wassermann negative.

Hospital Course: Two days following admission, the patient complained of intermittent abdominal pains every 5-8 minutes which resembled labor pains. It was thought that labor might aid in bringing the fetal head into the pelvic brim, but repeated attempts in the two hours after the onset of labor pains accompanied by moderately strong contractions were of no avail. The patient was premedicated with phenobarbital, grains 2, and sent to the operating room.

A fractional spinal procaine anesthetic was started. A midline incision was made below the umbilicus and continued through the fascia and peritoneum. A transverse incision was made in the visceral peritoneum about two inches above the uterovesicle reflection. The uterus was then opened transversely in its lower segment, membranes were ruptured and a normal nine pound, eight ounce male was extracted which cried spontaneously and was found to be in good condition. The placenta was removed and the uterine musculature was sutured with interrupted chromic No. 1 catgut and reenforced with a continuous chromic No. 1 suture. The lower peritoneal flap was sutured to the uterus above the uterine incision, to achieve peritonealization.

In repairing the abdominal wall, it was first necessary to trim away approximately four inches of skin on either side of the midline incision in addition to the firmly adherent underlying fascia and peritoneum. All bleeding points were carefully stopped. The peritoneum and transversalis fascia could now be easily identified, and were brought together with a continuous No. 0 plain catgut suture. The recti muscles were approximated with interrupted No. 0 plain catgut sutures. The external rectus sheaths were then imbricated by using interrupted chromic No. 1 mattress sutures to attach the right flap to the under surface of the left flap and a continuous No. 1 chromic suture was used to complete the overlapping procedure. The skin was approximated with interrupted nylon Stuart stitches.

Postoperatively, the patient's temperature rose to 102° F. and dropped to normal on the second postoperative day, remaining below 100° F. until the patient's discharge on the ninth postoperative day. Sutures were removed six days postoperatively with the wound healed by primary union.

The patient has been followed approximately one year and was last seen on Jan. 10, 1948. The abdominal wall was in good condition and there was no evidence of recurrence of the hernia.

DISCUSSION

In discussing this topic, Cartaya[3] observed that there are two causes which dispose a pregnant female to hernia. One is the relaxed, softened state of the muscle fibers with an excess of fluid in the tissues, and the other is the weight of the gravid uterus and the intestines.

Normal process of labor presupposes normal anatomical relations within the pelvic cavity and the abdomen. When these relations are in any way disturbed, the mechanical interference with the expulsion of the child is inevitable and this is precisely the situation which arises when ventral hernia, which is a mechanical defect, is exhibited in a pregnant woman. The force of the uterine contractions is either diminished or not exerted in the proper direction. The result is that labor is delayed and frequently cannot be terminated

until outside interference is brought into play.

Women who exhibit a marked separation of the recti muscles, either in the form of a simple diastasis which may have been a result of poorly managed previous pregnancies, or in the form of a true incisional hernia, are likely, especially if they are at all obese, to suffer from an aggravation of the defect during pregnancy.[9] It is, indeed, quite possible for the pregnant uterus, especially in the later months of gestation, to escape through the weakened abdominal wall and to sag below the symphysis.[4,10] If reposition is possible in such cases it is seldom permanent. No type of mechanical support is likely to be effective.[5] If the uterus can be returned to the abdominal cavity just before term, and if a presenting part can be forced into the pelvis so that the effect of the uterine contractions can be directed into the proper channels, vaginal delivery may be possible as was demonstrated by Saxtroph.

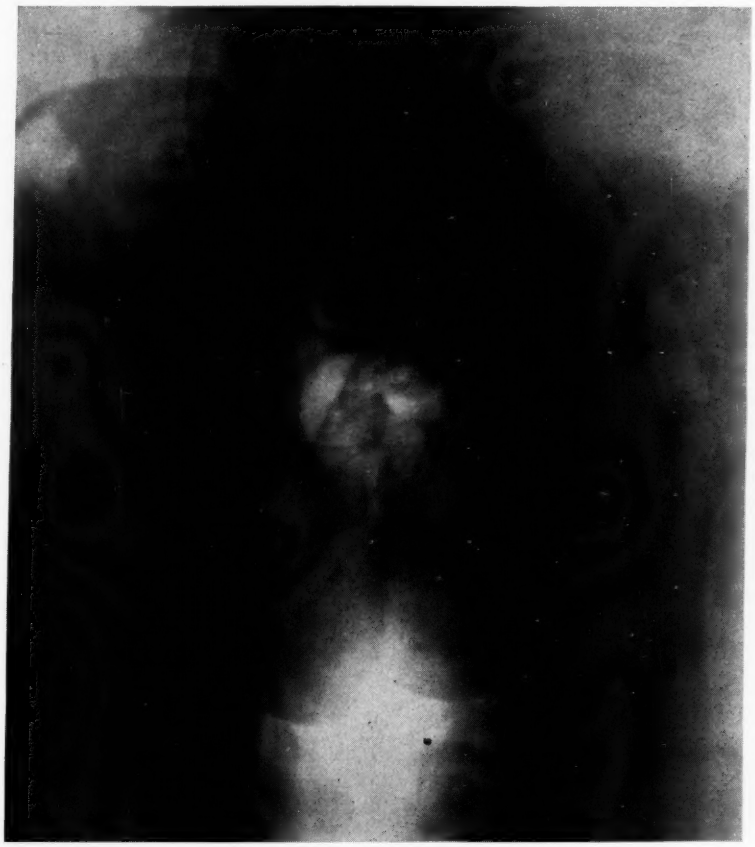

Fig. 2. Preoperative roentgenogram showing fetus superimposed on pelvis with breech in the dependent fundus of the uterus. (Compare with Fig. 1.)

A review of the literature fails to reveal whether or not herniation of the pregnant uterus occurs more frequently in patients who have had previous cesarean sections or other

lower abdominal operations. We feel, nevertheless, that meticulous repair of low abdominal incisions would tend to reduce the incidence of this condition in subsequent pregnancies. The cesarean section in the abovementioned case undoubtedly contributed to the formation of this hernia with her second pregnancy.

Since the literature reveals that obese women are more prone to develop this condition, the attending physician should do his utmost in attempting to prevent excessive weight gain in all obstetrical patients.

The pathology of this state may be due to the tearing of the recti muscles from their attachment or separation of the muscles from each other below the umbilicus, thus producing a diastasis.[3] Thereafter, there follows central bulging of the abdominal wall into which the pregnant uterus tends to gravitate. In this way, the entire anatomical relationship is changed, and the uterus assumes a dependent position. There is stretching of the round, broad, and sacrouterine ligaments which cause severe pain. The abdominal skin and fascia are greatly stretched, a condition which interferes with their normal circulation and nutrition. This results in an excoriation of the most dependent portion of the skin over the hernia and may complicate healing of the abdominal wound after repair if this area is not completely removed with the scar from the previous operation.

In retrospect, it is difficult to determine whether or not the wearing of a tight abdominal binder or corset during the first six months of pregnancy would prevent this condition from arising. It is not likely that, had the uterus been prevented from falling forward by sufficient abdominal support, herniation would have resulted. Had this been done, this patient might have been permitted to go into labor with a tight abdominal binder and deliver spontaneously from below. Since it was impossible to reposit the uterus so that the forces of uterine contractions would be directed downward through the birth canal, it was feared that the natural forces of labor would result in rupture of the uterus. Cesarean section, with reposition of the uterus and repair of the ventral hernia, was therefore chosen as the solution to this problem.

SUMMARY

A case of herniation of the gravid uterus through the abdominal wall after a previous cesarean section is presented. In this case it was felt that conservative management would have been the treatment of choice, had it been possible to reestablish relatively normal anatomical relationships. It is also felt that proper abdominal support throughout pregnancy might have prevented this condition. Since it was impossible to correct the malposition of the uterus and fetus sufficiently to permit normal labor and delivery fom below, low-flap cesarean section was performed with reposition of the contracted uterus and repair of the ventral hernia.

RIASSUNTO

Descrive un caso di ernia dell'utero gravido attraverso la cicatrice di un precedente taglio cesario. Un opportuno sostegno addominale durante la gravidanza avrebbe probabilmente prevenuto quest'incidente, mentre un intervento operativo avrebbe potuto essere evitato qualora fosse stato possibile ristabilire dei rapporti anatomici relativamente normali. L'impossibilita' di correggere la malposizione dell'utero e del feto in modo da permettere un parto normale per la via vaginale ha costretto invece l'A. ad eseguire un taglio cesareo sul segmento inferiore, seguito da una ricostruzione plastica delle pareti addominali.

SUMARIO

El autor presenta un caso de hernia del utero gravido por la pared abdominal resultante de una operacion cesareana previa. En este caso quizas hubiera sido posible un tratamiento conservativo con el uso de un soporte abdominal apropiado durante todo el curso del embarazo que hubiera evitado la hernia. Sin embargo la existencia de la hernia y la imposibilidad de corregir la mal-position del utero y del feto lo suficiente para permitir un parto normal, requirio el tratamiento quirurjico de operacion cesareana baja con reposition del utero contraido y reparacion de la hernia ventral.

SOMMAIRE

Un cas de hernie de l'utérus gravide à

travers la paroi abdominale, consécutif à une section césarienne est présenté. Dans ce cas le traitement conservatif aurait été de choix, s'il avait été possible de rétablir les rapports anatomiques normaux; nous sommes aussi de l'opinion que si un support abdominal avait été employé durant la grossesse, cette condition ne serait pas survenue. Comme il était impossible de corriger la mal-position de l'utérus et du fétus suffisamment pour permettre un accouchement normal et une délivrance par en-bas, nous fîmes une incision césarienne suivie de réposition de l'utérus et de réparation de la hernie ventrale.

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INFORMAL DINNER FOR MEMBERS OF THE
INTERNATIONAL COLLEGE OF SURGEONS,
THEIR WIVES AND GUESTS
during the meeting of the American Medical Association
Atlantic City, Thursday, June 9, 1949, Strand Hotel
Reception 5 P.M. promptly Dinner 6 P.M. promptly

Adjournment 9 p.m. promptly to afford ample time for those
desiring to attend the reception for the
President of the American Medical Association

Editorial

Doctors of Infamy: An Editorial Book Review

A COMPLETE and fully documented account of the medical and surgical crimes perpetrated by German physicians and surgeons under the Nazi political regime during World War II is now available in "Doctors of Infamy," a book newly released from the presses of Henry Schuman, New York. The authors are Dr. Alexander Mitscherlich, head of the German Medical Commission to U. S. Military Tribunal No. 1, Nüremberg, and Fred Mielke.

Professor Andrew C. Ivy, M.D., vice-president of the University of Illinois and medical scientific consultant to the Prosecution at the same tribunal, contributes a telling introduction based on his personal investigation of the facts. Brigadier General Telford Taylor of the U. S. Army, chief of counsel for War Crimes, adds a judicial and condemnatory statement clearly setting forth the legitimate limits of experimental work in the medical field and the utter disregard of principle with which these limits were violated. Dr. Leo Alexander, psychiatrist and consultant to the secretary of war and to the chief of counsel for War Crimes, discusses the attempts of the Nazi scientists, in collaboration with Reich political authorities, to cover the ruthless destruction of racial groups and handicapped persons under the mask of scientific research. A note on medical ethics in general is contributed by Albert Deutsch, who includes in his presentation the new Hippocratic Oath as adopted by the World Medical Association. The main body of the book has been translated from the German by Heinz Horden.

This material, gathered by men of indisputable authority in their fields and supplied with incontrovertible evidence from Nazi letters and directives, many of which are quoted in full, lends new force to the proclamation of the World Medical Association condemning not only the men who took active part in the incredible slaughter but the doctors who gave it their tacit support by silence. Briefly, this proclamation covers the following points:

1. Solemn condemnation of the crimes committed against humanity by German medical practitioners and endorsement of the judicial punishment of the criminals.
2. Invitation to representative German medical organizations to make public admission of guilt, pledging themselves to future respect of human personality, dignity and freedom.
3. Re-emphasis on the need of eternal vigilance on the part of all doctors and full recognition of the influence of medicine on society in general.
4. Re-emphasis on the need of maintaining throughout the medical curriculum the traditional aims and ethics of medical practice.
5. Recommendation that a uniform oath or promise based on the spirit and content of the Hippocratic Oath should be subscribed to by every medical practitioner on receiving his medical degree and his license to practice.

The Journal of the International College of Surgeons wholeheartedly subscribes to all these propositions and also to revision and extension of the Hippocratic Oath to include formal recognition of the rights of all human beings, regardless of color, race or creed. The *Journal* also recommends to physicians and surgeons a careful study of the actual facts as set forth in this book which bears witness to the foulest hypocrisy, as well as the cruelest butcheries, ever recorded of man.

"Doctors of Infamy" is not a large book, as books go. It contains not quite two hundred pages in all. But the civilized reader, turning these pages over, cannot escape the feeling that his fingers dabble in blood. Here are the facts, attested to and proved. In the clean name of science, thousands of helpless and inoffensive men, women and children were violated, maimed, blinded, beaten, starved, frozen, tortured to death with thirst, decap-

tated, and buried or burned alive, not by an infuriated mob but by cool-minded scientists and accredited healers who directed the whole debauch with a stop-watch in one hand and a notebook in the other. Day after day these doctors murdered their quota; night after night, quite undisturbed in mind, they returned well satisfied to the Gemütlichkeit of family life or professional comradeship. In all the bloody history of the world there has been no such record till now.

We have fondly believed that man's barbarous days were ended. We have seen him marching slowly but steadily upward, discarding one by one his bestial vices, his uncontrolled animal appetites and ferocities. We have seen him learning to follow the light of the mind. Now in a moment, in the twinkling of an eye, we are compelled to see that torch blown out and to witness the naked anguish of a continent darkened and writhing in primitive fear. The maxim, "Forgive them, for they know not what they do," has no application here. The German doctors knew very well what they did. They had spent their lives and energies learning to do it. They did not scruple to add to the violence of murder and mutilation the subtler treason of deliberate infection of prisoners with deadly disease. More, they delighted in it and spoke of it proudly.

For the sake of a collection of the skulls of Jews—"a repulsive but typical species of subhumanity"—these human jackals *processed* in a single experiment one hundred and fifteen human beings of both sexes. *Processing* consisted of murdering these persons with lethal gas, detaching their heads from their bodies, packing the severed heads in airtight containers and shipping them to headquarters to be denuded of flesh, classified and ticketed like exhibits in a museum. In an experiment on animal heat, men were stripped naked, chilled to unconsciousness and placed between the bodies of naked women, and the time it took to restore them was carefully noted. This engaging experiment was reported almost genially by the observers. Other freezing experiments, sometimes with simultaneous starvation, were conducted on a massive scale. The victims begged to be shot, but the doctors were obdurate.

Vacuum and pressure chamber experiments were made to determine resistance to high altitudes. A typical experiment "on a Jew aged 37, in good condition," resulted in death at the end of half an hour. Electrocardiographic tracings were taken every five minutes and recorded the victim's agony and death. Rascher, who was in charge, reported proudly: "This is the first case of its kind to be observed in man. The experiments are being continued and expanded."

In experiments on making sea water potable by chemical treatment, prisoners were tortured by thirst and starvation to a state of insanity; many of them lapped like dogs at the filthy water used to scrub floors. Those who became delirious were tied to their beds. Symptoms of heart trouble were coldly observed and duly recorded.

The inoculation experiments were gruesome almost beyond comprehension. One large group of victims underwent infection with typhus for the sole purpose of keeping a supply of typhus-infected blood available. Dr. Kogon commented, with a trace of irritation, that nearly all of them died. But this lack of cooperation, though annoying, was not disastrous; there were plenty of other victims ready to hand. Plenty of Jews and human beings of other religious beliefs of both sexes; plenty of helpless prisoners to be given typhus, tetanus, cellulitis and infectious jaundice and to scream out their pitiful lives without mercy or help, in order that the great new therapy of the Master Race might come to its speedy fruition.

Gas also, being a potent weapon of war and an excellent agent for the extermination of "undesirables," was given exhaustive and appalling tests. The agonies of prisoners treated with mustard gas are described in such a manner as to be nearly unreadable. "After about ten hours . . . burns began to appear all over the body. . . . Some of the men went blind. . . . The pains were so terrific that it was almost impossible to stay near these patients." Nevertheless, be it noted, all the burns of all the patients were photographed every day. In those who died, autopsy revealed the liver and inner organs completely eaten away.

Experimental surgery enjoyed a prolonged field day, with unlimited material at hand for

fractures, bone grafts, amputation and wound infection. The operating table became an instrument of mutilation and murder. Legs of victims were broken with a hammer in several places and left after a day or two without casts, to heal as best they might. Various pathogenic bacilli, notably those of tetanus, were introduced into the wounds; so also were fragments of wood and slivers of glass. Nerve sections were removed and the results recorded. Bone slivers and segments were liberally intertransplanted. Patients mutilated beyond repair were quickly disposed of by lethal injection. Injection, in fact, of any one of several swiftly lethal agents (notably benzene) was a favorite device; it was relatively inexpensive, and it cleared out the wards with admirable speed, so that other victims might not be keep waiting too long.

The tissue of lies and hypocrisy on which this wholesale slaughter was based is obvious throughout, since not one of these blood-curdling experiments resulted in the slightest gain to medical science. But from the standpoint of intellectual corruption the infamy reached its zenith in the race-destroying programs of murder and sterilization. The ghastly mass killings and mutilations in these categories were based overwhelmingly on "unfitness" due to nothing more than the misfortune of belonging to an unfavored racial or religious group. Euthanasia, by the way, acquired a new definition in the process, for it would be difficult to describe these deaths as easy. Extermination of the Jews and others of political beliefs different from the Nazi doctrine was the central purpose, and even the fanatics who desired it most could not deceive themselves into believing that there was any scientific purpose behind the massacre. The murder of aged and enfeebled persons and of young children with congenital mental or physical defects had long been a part of Hitlerian economy. Peculiar Nazi logic.

In the course of the murderous program, wards full of children were simply left to starve. Men and women in droves were disposed of by gassing. Elaborate medical histories and records were kept, but in the case of any Nazi-rejected person the flimsiest conceivable excuse was enough to warrant the death sentence.

The destruction program, said one of the doctors concerned, was a purely routine job. "Of this new instalment (Jews) I managed to do seventeen today; Müller fifteen," he reported. At 5 P.M. sharp we 'downed tools' and went to dinner." It is not to be doubted that after such labors they enjoyed their meal.

Sterilization was performed ruthlessly upon thousands of men and women, either by roentgen ray treatment or by surgical means. Most of the victims were driven back to slave labor immediately afterward, in spite of their excruciating pain. Some of them, unable to walk, fell down; these were dragged back and gassed.

The results of all sterilizing procedures were checked with painstaking care. SS Lieutenant Brandt was particularly anxious. In a written directive he suggested that, in case of doubt, it would be well to "lock up a Jewess with a Jew for a certain period of time, any success attained to be reported."

The total callousness with which these doctors regarded the suffering of their victims is glaringly evident. Their casual manner of referring to the matter suggests that they were speaking of vermin, not human beings. "I did not trouble about what would be done with the bodies of the inmates I had poisoned," said one, and another answered in response to a question in court, "I paid no attention to the nationality of the murdered inmates." With unexampled hypocrisy the Nazi authorities sent unctuous "regrets" to the bereaved families following them up a few days later with a container purported to hold the ashes of the loved one but actually filled with ashes shoveled up at random from the crematory floor. It is difficult and also time-consuming to select the ashes of any particular corpse from a heap containing the ashes of several others.

Twenty-three of these criminal physicians —by no means the total number—were brought to trial. Only a few of the lower-ranking ones showed any uneasiness of conscience. The arch-fiends were as bland and complacent as ever. "I served my Fatherland," said Brandt, "as others before me."

One is forced to admit a tragic truth in his words. The Fatherland has been served by many like him, not only in the recent war

but in that which preceded it. The appalling feature of the situation in World War II is that these men were doctors, and that they had the tacit connivance of the whole German medical profession behind them. Not one effective voice was lifted in protest. The fact that not all German doctors took an active part does not and cannot exempt them from guilty responsibility, as the World Medical Association has pointed out.

Physicians all over the world, shocked beyond expression by these monstrous and innumerable desecrations of the medical ideal, have found themselves at a loss to express their horror. If after so many centuries of struggle, persecution and martyrdom the medical profession itself, which has had to fight every step of the way for recognition and achievement, can fall so swiftly and easily to such barbarous depths, it is hard to reaffirm one's belief in man's power to escape the vestigial beast within him. Could it happen here, this infamy? Are these among us, here in American towns, doctors who are capable of this treason to their fellowmen? Would political pressure strip them of culture, wisdom and decency and turn them in a moment from men to murderers? Could one foul breath of tyranny blow out the light?

These are grave questions indeed, but they must be faced. The state of the world today is more than alarming. Only by the strictest adherence to the original ideals of our profession can we hope to retain the confidence of those we serve. Only by pledging ourselves anew to the art of healing, without discrimination, all those who come within the sphere of our ministrations, can we keep our self respect as men and doctors. In these complicated times there are already many barriers —some necessary, some unavoidable—between physician and patient. The traditional intimate relation is hard to maintain. But when that tradition goes, disaster will follow; and the possible magnitude of that disaster can be seen in the pages of this book as in a mirror. The difference between a decent physician and these Nazi animals is altogether a difference of mind and spirit, and it behooves us to examine in ourselves the condition of both, not once but repeatedly. Moral disintegration, like cancer, is sometimes asymptomatic at first.

Needless to say, the young men and women now coming into the practice of medicine and surgery must be safeguarded from the beginning. To this end the World Medical Association recommends the administration of the new Hippocratic Oath to every candidate for a professional degree:

> "Now being admitted to the practice of medicine, I solemnly pledge to consecrate my life to the service of humanity. I will give respect and gratitude to my deserving teachers. I will practice medicine with conscience and dignity. The health and life of my patient will be my first consideration. I will hold in confidence all that my patient confides in me.
>
> "I will maintain the honor and the noble traditions of the medical profession. My colleagues will be as my brothers. I will not permit consideration of race, religion, nationality, party politics or social standing to intervene between my duty and my patient. I will maintain the utmost respect for human life from the time of its conception. Even under threat I will not use my knowledge contrary to the laws of humanity.
>
> "These promises I make freely upon my honor."

This is much in line with the admonitions on the diploma for Fellowship of the International College of Surgeons, designed and worded by Dr. André Crotti:

> "Be aware that the life and health of your patients depend upon your knowledge and your conscience.
>
> "Never allow material and personal gain to become the guides of your conduct.
>
> "Remember that your duty is to seek constantly your professional perfection.
>
> "Also, never forget your obligations to your colleagues."

Thus the World Medical Association and the International College of Surgeons have much in common.

The need for the revision of the Hippocratic Oath is in itself a sad commentary on present-day civilization, for all the promises it contains were implied in the original Oath of Hippocrates and should have required no emendations. Nevertheless it is well that the

additions have been made, for no precaution can be too great to take in the prevention of another major medical debacle. The young physician or surgeon just entering practice will take this oath at a time when, it is to be hoped, he is still ardently imbued with the practical idealism of the genuine physician, and before corruption has had an opportunity to attack him. The more specific the promises he makes, the greater the probability that he will keep them. As the British Medical Association has pointed out, neither the science nor the practice of medicine can be separated from the external moral values.

The profession has always had a profound effect upon the state of society in general. How can it be otherwise? Society is the doctor's field of work. In the human relations with which he must deal daily—relations with his patients, his colleagues, his aides and the world in general, he wields an influence, both by precept and example, that can only be described as tremendous. As a physician or surgeon he is dedicated entirely to the best interests of his patients; as a teacher, to the soundest possible guidance of younger men; as a scientist, to the most devoted study and research, followed by the generous sharing of his discoveries with colleagues who may find them useful; and as a human being to the moral and spiritual verities he has learned from his preceptors, his experience, and his acquaintance with the great minds of the past.

These responsibilities are essential to the health of the medical profession. Without them, nothing significant can be accomplished; and the absence of any part of any one of them will inevitably create a vacuum, to be filled sooner or later with some form of corruption. *The Journal of the International College of Surgeons* urges everyone connected in any way with medicine or surgery to support the program of the World Medical Association and recommends that every man who has had or expects to have the life of a human being in his hands to read every word of "Doctors of Infamy," that he may know the full measure of his task and the high responsibilities it entails.

MAX THOREK

News Notes

Full Approval Given to Chicago Medical School

The American Medical Association and the Association of American Medical Colleges granted full approval to the Chicago Medical School, Nov. 9, 1948. Announcement of the approval was made at White Sulphur Springs, Va., where the Association of American Medical Colleges was holding its annual meeting. The A.M.A. Council on Medical Education and Hospitals met simultaneously to take joint action of full approval for the school.

The Third Peruvian Congress of Surgery

The Third Peruvian Congress of Surgery will take place in March 1949. The following papers will be considered: Surgery of the Bile Ducts, Osteomyelitis and Gastroduodenal Ulcers. Regulations for joining the Congress are put forth and those interested are requested to contact Dr. Luis M. Delgado, Camana 773, Lima.

National Research Council Enters Fight Against Alcoholism

Under the leadership of Dr. Anton J. Carlson, Chicago, president and scientific director of the Research Council on Problems of Alcohol, the organization has spearheaded in medical schools and other scientific institutions investigations into the causes and treatment of problem drinking. At a special meeting, the Research Council voted to turn over its research operations and assets to the National Research Council of Washington, D. C. Also the public informational and educational publications would be turned over to the Division of Mental Hygiene, U. S. Public Health Service. Both national organizations have agreed to accept the pertinent assets and carry on the work of the council.

United Nations Nutritional Survey

A report covering a six month investigation of conditions in Austria, Czechoslovakia, Greece, Hungary, Italy, and Rumania revealed a more acute situation for outside nutritional help and relief than a year or two ago. Conditions are attributed to three causes: lack of safe-quality domestic milk supplies; slaughter of dairy herds and the failure of food and animal-feeding crops as a result of previous droughts. All six countries are below recommended standards for adequate nutrition, and there is a general chronic shortage of foods of animal origin.

Who to Administer International Prizes

The assets of the Leon Bernard Foundation have recently been turned over to the World Health Organization, and will be administered by the director-general. This Foundation periodically awards the International prize for practical results shown in social medicine, and The Expert Committee on Social Medicine, which is appointed by the Health Assembly will select the prize-winner. The World Health Organization will direct the International Malariology Prize. This prize is awarded by the Darling Foundation to the author of an original study on pathology or prophylaxis of malaria. The candidate for the medal and prize is to be recommended by The Expert Committee on Malaria. The Leon Bernard Foundation which is in memory of Professor Leon Bernard was established in 1937, and the Darling Foundation, in memory of Dr. S. T. Darling was created by prize funds in 1945.

The Third Congress of the Inter-American Radiology Society

The Third Congress of the Inter-American Radiology Society will hold its annual meeting in Santiago de Chile, November 1949. An invitation has been extended to all radiologists to participate in the scientific event. Subjects tentatively on the program include: Radiologic Exploration of the Cardiovascular Compartments with Contrast Media, Diagnostic and Exploratory Radiology of the Cranium, and Treatment of Cancer of the Uterus.

Delayed Nobel Prizes

Due to Nazi government prevention, the Nobel prizes are just now being awarded. Professor Richard Kuhn and Professor Adolph Butenandt are now to receive the prizes.

The work of Professor Butenandt, who in 1939 was director of the Kaiser Wilhelm Institute for Biochemistry has had important results for medicine. After serving his apprenticeship under Windaus, at Gottingen, he went to the chair of chemistry in the then free city of Danzig, and later to the Kaiser Wilhelm Institute to fill the chair vacated by the removal of Neuberg. German

workers were quick to recognize the implication of the findings of Aschheim and Zondek and Professor Butenandt was supplied with large quantities of extract of the urine of pregnant mares for the isolation of the oestrus-producing hormone. Interesting and important papers began to come from his laboratory. His brilliant degradation work demonstrated clearly the constitution of oestrone. Later he made fundamental contributions on the constitution and partial synthesis of progesterone and the isolation and characterization of androsterone.

Professor Butenandt on several occasions before the war lectured in English in the University of London.

Anti-TB Drive in India

The first nation-wide BCG vaccination campaign in India was officially inaugurated at Madanapalle, near Madras. The campaign was launched for the purpose of trying to lower the rate of tuberculosis among children and adolescents, and is to be carried out jointly by the Indian health authorities and the World Health Organizations. It was these authorities which last May sent a medical team of tuberculosis experts to India at the government's request. Since transportation of BCG vaccine from Europe was unreliable, WHO also sent India a pharmacologist to assist in starting the laboratory. The laboratory now produces the vaccine.

The population of India is estimated at 320,000,000 and the number of TB cases at 2,500,000 with 500,000 deaths occurring each year.

The Indian program is part of the global anti-tuberculosis campaign which WHO is giving priority to for 1949.

Nazi Persecution of Scientists

Dr. Walter C. Alvarez, Mayo Clinic, *Science*, **109**:122, believes that Goebbels comment in "Goebbels' diaries" should give poise in times of peace to political machinery in its effort of baiting scientists and great men. Goebbels tells of an occasion on which he, Frick, and Rust were guests of the Fuehrer. He wrote, "Their comments and remarks were so idiotic as to reveal how completely out of the picture they really are. They delivered themselves of stupid phrases. . . ." The important point is that Rust was the Nazi Minister of Education and had been an inmate of an insane asylum. He was the one chosen to persecute the scientists and university leaders causing them to flee from Germany for their lives. In his devotion to his Fuehrer, Goebbels tried to make him out as a would-be patron of science, ignoring the fact that he had appointed a miserable quack as his private physician.

In speaking of the critical situation of the submarines in the face of the new detecting devices developed by Allied physicists, Goebbels wrote, "It is the fault of Rust and is irremediable. . . . The mediocre talents in the Reich Government are a wall between the Fuehrer and many sectors of public life. Our technical development both in the realm of submarines and of air war is far inferior to that of the English and the Americans. We are now getting the reward for our poor leadership on the scientific front, which did not show the necessary initiative to stimulate the willingness of scientists to cooperate. You just can't let an absolute nit-wit head German Science for years and not expect to be punished for such folly."

Putting men of science in their places is great fun for politicians but Goebbels has told us how disastrously this policy pays off when war comes.

World Program of Disease Prevention

In China, the International Health Division of the Rockefeller Foundation has started a program of malaria control and research on typhoid fever. In Peru special studies on the development of local health services have begun. Yellow fever is being studied under the auspices of the Division in East and West Africa, as well as some South American countries. Malaria is being discussed in Italy and Sardinia, the Netherlands, the West Indies and South America.

One rather ominous feature in connection with malaria control measures instituted in Italy was that after a D.D.T. house-spraying campaign in a coastal region north of Naples and in the Tiber delta, it was found that house flies were not affected. Apparently a race of flies abnormally resistant to D.D.T. has become predominant in those areas and also in other regions of the mainland where the insecticide has been in use for several years. While the general sanitary value of the spraying is lessened, thus far all varieties of anopheline mosquitoes remain susceptible to D.D.T. and malaria transmission rates continue very low.

Typhus fever and testing of para-eminobenzoic acid in treating louse-borne infection have received special consideration. Work is also being done on mice to find chemicals of value against scrub typhus.

New Books

Cancer of the Esophagus and Gastric Cardia. Edited by George T. Pack, and contributors. St. Louis, The C. V. Mosby Co., 1949.

This book comprises the subject matter which originally appeared in *Surgery,* June, 1940. The articles deal with carcinoma of the cardiac region of the stomach and carcinoma of the esophagus. The esophageal carcinomata are dealt with in separate sections which concern the cervical, middle and lower portions of the esophagus.

In the discussion of cancer of the cervical esophagus, a series of 77 cases is reported in which 11 (14 percent) were operable. In seven of the operable cases (64 percent) the tumor was resectable. Of the seven patients in whom the cervical esophagus was reseeted, one patient died on the second postoperative day of cardiopulmonary complications; the other six patients survived the operation and had a rather uncomplicated course. Four of these latter patients were alive seven years, one year, nine months, and six months after surgery; none of these showed recurrences. Two were alive with recurrences three years, and three months after resection.

Rotation roentgen therapy as practiced by the Scandinavian school of radiologists is discussed. The statistics of Dr. Jens Nielsen suggest that this type of therapy might have a place in the treatment *per se,* as well as palliation of carcinoma of the esophagus.

Many sections are devoted to the various anastomoses, both supra and infra-aortic.

This book will be useful for all those interested in the subject of esophageal carcinoma, and can be recommended to those who desire information concerning the modern management of these previously inoperable lesions.

Surgical Pathology. By P. A. Herbut, M.D. Pp. 710. Philadelphia, Lea & Febiger, 1948. $12.00.

The publication of this work marks the arrival of a newcomer into the literature devoted to surgical pathology. The book has been designated primarily to aid candidates for the higher degrees in surgery, and also surgical pathologists who desire a brief review of their subject. After a perusal of the text, we thoroughly agree that the author has admirably succeeded in his purpose.

The material has been discussed on a purely regional basis, or to be more specific, the classification of the subject matter is systemic—a plan frequently adopted in most works on surgical pathology. Each chapter is preceded by a brief account which highlights the essential features of the normal histology, anatomy, and embryology of the topic under discussion.

The illustrations are adequate, although the clarity in reproduction of some of the microphotographs are not as successful as one would desire. There are no colored plates.

The pathology of the nervous system is omitted, as are discussions on such general considerations as inflammation, repair, tumors, infection, hemorrhage, thrombosis and embolism. But those systems which are covered are presented in an up to date, comprehensive manner. This book will undoubtedly enjoy a wide market.

Osler as a Gastroenterologist. By Felix Cunha, M.D. San Francisco, Times-Star Press, 1948.

The figure of William Osler, whose life, work, teachings and personality have inspired thousands, has seldom been depicted with such appreciation than in the pages of this volume. Dr. Cunha's treatment presents him at full stature, with admiration for his skill, wisdom and energy and with due reverence for his outstanding personal qualities.

The frontispiece, a singularly appealing portrait of Osler, corroborates Dr. Cunha's enthusiasm. The face shows evidence of his humanity as well as his shrewdness and power. It is a face that inspires instant confidence, and as we proceed through the ensuing pages with their wealth of quotation, anecdote, allusion and reminiscence, we are impressed anew with the extraordinary breadth of the Oslerian outlook on life and learning.

An inveterate reader, Osler persistently urged his students to read. He himself, in his early youth, was deeply and permanently influenced by Sir Thomas Browne's *Religio Medici.* Dr. Cunha expresses the opinion that this book was the foundation of his later philosophy. Obviously he never forgot it or ceased to reread it, for he owned a first edition which was laid on his coffin at death. A book collector's item not kept under glass but thumbed and worn from its owner's constant use.

His other reading was both wide and varied, not confined to medical literature. On the contrary he protested early and vigorously against medical chauvinism, the attitude of mind that leads a doctor to despise and disregard "anything outside his own school or circle."

This habit of far-ranging study, together with a natural disposition toward humanity contributed notably to the lasting value of all Osler's writing

and especially to the world-wide popularity of his famous *Practice of Medicine*, which has been read with delight by laymen as well as by physicians. "No other book of science," comments Dr. Cunha, "ever so quickly gained its popularity and maintained it." The book is enlivened throughout with well chosen and pointed literary allusions, which, in combination with Osler's own witty and lucid style, makes excellent reading.

Gastroenterology was a subject of immense interest to Osler. His first contribution to this branch of science was made unwittingly when, as a student in Toronto, he was assigned a postmorten study of a huge sacculated aortic aneurysm. Young Osler's attention was caught by the extrinsic pressure on the esophagus. Later he was to write countless papers on gastroenterologic problems: ulcers of the stomach, pylorus and duodenum; hepatic cirrhosis, especially the ascitic phase; tumors of the gastrointestinal tract; gallstones; peritonitis; pyloric stenosis, and an almost limitless succession of other conditions.

"Hardly any aspect of pathology," says Dr. Cunha, "escaped his scrutiny and attention." He did exhaustive studies on trichinosis, and published important descriptions of diagnostic exploratory technics in detecting cancer of the stomach long before roentgen ray diagnosis was available. Even after Roentgen's discovery he stoutly maintained that in certain cases a positive diagnosis could be made only after an exploratory laparotomy.

Osler was a prolific writer and had prodigious energy throughout his working life. "There was never to be any lying abed till noon for Osler. . . . The foundation upon which his life was built was work. If one were to measure his activity by the number of published papers, then the years 1895, 1896 and 1897 were the most prolific. However, during his entire active writing career he managed to get together an average of 30 papers a year, plus five pathological reports, five educational addresses and about the same number of book reviews. . . . One can only say that he must literally have lived, eaten and slept with medicine, for he did not employ a ghost writer."

Generations of readers will be thankful that he did not. His own pungent style adds enormously to his writing. Some of his aphorisms are unforgettable. "If you see anything that you know is true, begin to doubt it at once. The mental kidney, more often than the abdominal, is the one that floats. The value of experience is not in seeing much but in seeing wisely." These are the comments of a man aware of all human fallibility, who did not hesitate to ascribe that fallibility to physicians and who never forgot its existence in himself.

His humanitarian attitude is summed up in a little masterpiece of advice: "dealing as we do with poor suffering humanity, we see the man unmasked, exposed to all the frailties and weaknesses. . . . Keep a looking glass in your own heart . . . the more carefully you scan your own frailties the more tender you are for those of your fellow creatures."

This book is a refreshment to the spirit as well as to the mind. The steadfast practical idealism, the optimism uncluttered by fatuity or self-deception that were so characteristic of Osler are needed today. The great medical minds of the past, whether recent or remote, have much to offer physicians of today. Not least among the giants is William Osler, whose mind and motives are represented here.

The Lung. By William Snow Miller, M.D. Ed. 2. Pp. 222. Springfield, Ill., Charles C Thomas, 1948. $7.50

This is essentially a treatise on the gross and microscopic anatomy of the lung, and represents over 50 years research by a single worker, although credit is given to many other workers.

Early in 1887 Dr. Miller became interested in the anatomy and pathology of the air spaces in the lungs, inspired by Dr. Francis Delafield and J. West Roosevelt. Further studies followed in Leipzig and Johns Hopkins. Data accumulated and it was not until 1937 that the first edition of this work was published. A second printing was made in 1940, followed by a third in 1943. These were reprintings, not new editions. This second edition has been published simultaneously by the Ryerson Press, Toronto, Canada.

The surgeon will find nothing here regarding diseases of the lungs; therefore no technics for removal of a lobe, for thoracoplasty or for other procedures. Nevertheless, it is well for one to review the anatomy of blood vessels and lymphatics in order to understand pulmonary pathology. Lymphatics form a closed system and do not connect with connective tissue spaces, nor with the pleural cavity by means of stomata. No lymphatics are present in the walls of the air spaces distal to the ductuli alveolares, but the larger bronchi possess two sets of lymphatics. One may thus have a better understanding of metastases.

There are 255 references in the bibliography. The index might have been improved by separating subject and author instead of running them together. This is in the interest of quick and easy reference.

Only an investigator who has a tremendous capacity for detail can write down his observations as Dr. Miller has done. He seems not to have missed a single point in the mastery of his subject.

Textbook of Anaesthetics. By R. J. Minnitt and John Gillies. Ed. 7. Pp. 568. Baltimore, The Williams and Wilkins Co., 1948.

This well known British work has of late been receiving increasing attention among American students of anesthesia, and it is to be expected that this edition will receive widespread dissemination on this side of the water. For this book has progressed considerably since its infancy, when it was known as a *Handbook of Anaesthetics*. This excellent textbook is the product of a wide range of subject matter and a comprehensive treatment applied to the material by the authors.

The bulk of the book deals with general anesthesia, but there are adequate accounts on conduction and intravenous anesthesia. In addition, there are new chapters on the uses of curare, and the therapeutic applications of oxygen, helium, carbon dioxide and nitrogen. A final chapter is devoted to medicolegal aspects, which should be read by all medical men who earn their livelihood in the operating pavilion.

This book is recommended as one of the better short works on anesthesia.

Lives of Master Surgeons. By Richard A. Leonardo, M.D. Pp. 469. New York, 1948. Froben Press, Inc. $6.00.

This book was designed as a companion-piece of an earlier work, *History of Surgery*, written by the author in 1943. Essentially, it consists of thumbnail biographies of surgeons—some famous, some obscure—past and present. Only deceased men are included. The arrangement of names is in alphabetical order. This work should prove useful as a quick source of reference for historians and other interested readers.

Atomic Energy. Karl K. Darrow, Ph.D. New York. John Wiley & Sons, Inc. $2.00.

These four lectures were designed for people who understand the language of physics but whose special fields lie elsewhere. The object was to develop and stress the salient features pertaining to the transformation of energy of rest mass into energy of motion and energy of heat—a concept which is meant by "atomic energy."

Some of the concepts are not easy to believe. Precise assertions are made about the ultramicroscopic "astronomical-like" structure of these tiny bodies: that they circle and spin; that they make collisions with each other which simulate the characteristics of a traffic accident; that they defy ones motion of "the solidity of solid matter and the deadness of dead weight."

Atomic structure is explained in terms of the protons, neutrons, and electrons which comprise the nucleus of the atom. Darrow differentiates between an ordinary chemical reaction and a physical change in the structure of the nucleus itself. Thence, he leads the reader to more complex subjects: what isotopes are; how the scientist can bombard the nucleus and force it to transmute itself into the nucleus of another element; what radioactivity is; and, finally, how man has developed and unloosed the self-perpetuating chain reaction.

Simple analogies help the reader grasp the basic principles of nuclear theory and the atom's characteristics of weight, mass and energy. Numerous illustrations make the discussion doubly clear.

What has already been done in this field is one of the monumental achievements of all time. There is promise of much more. On the side lines physician and surgeon eagerly and anxiously await the application of this knowledge to the cure of neoplastic, and other forms of disease.

The Clinical Management of Varicose Veins. By D. W. Barrow, M.D. Pp. 155. New York, Paul B. Hoeber, Inc., 1948. $5.00.

There are few surgical conditions which have received as much ill-merited lack of consideration as the disease entity known as varicose veins. Hurriedly glossed over in the surgical curriculae of most medical schools, dallied with by the general practitioner, and frequently neglected by the busy surgeon, varicose veins have not always received the precise, active treatment which they call for. It is therefore most fitting that this monograph on the subject appear, for herein, the author has ably covered the entire gamut of the disease with its frequent complications.

The order of presentation of the subject material is logical, starting with the anatomy and physiopathologic aspects, then proceeding onto the symptomatology, the diagnostic tests most frequently used with their interpretations, and finally the suitable therapy. The text is comprehensive but succinct.

The diagrams are clear, and the entire work will be readily understood and appreciated by anyone seeking thorough information about the distressing condition of varicosities of the lower extremity.

Abstracts from Current Literature

Atypical Crohn's Disease. Bennett-Jones, M. J. and Wigglesworth, G. F., *Brit. J. of Surg.*, July 1948, **36**:65.

In 1932 Crohn, Ginsberg and Oppenheimer first described 14 cases of regional ileitis, recognizing it as a pathological entity. In America, by 1937 over 200 cases had been recorded in most of which Crohn's original description was found to apply. The disease is usually maximal in the terminal ileum, but we now recognize that the cecum and ascending colon may also be involved. The inflammatory phase is occasionally encountered by surgeons because of signs and symptoms suggesting appendicitis. Many of these cases have remained symptom free for a year. The obstructive phase of the disease is less common and sometimes associated with internal or external fistulae.

Taylor (1945) stated that Crohn's disease could not be distinguished from hypertrophic ileocecal tuberculosis by means of clinical features or morbid anatomy. He presented three cases, two of which died from miliary tuberculosis. Tubercle bacilli were found in resected specimens which simulated Crohn's disease.

The authors present three cases in which tuberculosis is definitely ruled out by culture and stained sections.

The first case is atypical owing to the size of the mesenteric glandular enlargement. There was central necrosis, rupture, and peritonitis. The second case was unique. There was repeated swelling of the right buttocks with sciatica, fever, limitation of motion suggesting tuberculosis of the hip. Abdominal symptoms were minimized. A rectal examination disclosed a pelvic abscess which was opened by the examining finger. Operation disclosed an inflammatory mass in the pelvis involving the terminal ileum, cecum and appendix. Because of the patients poor condition an anastomosis was made around the mass. At a later operation 2 feet of terminal ileum and the right colon were removed and a fistula into the rectum was closed. Seven months later this man was well and strong and working.

The third case is unusual in that only the cecum was affected. The right half of the colon was resected with only enough of the terminal ileum being removed to permit anastomosis. She is well after eight and a half years.

VICTOR T. HUDSON

Etiology of Acute Pancreatitis. Lium, R., and Maddock, S., *Surgery*, 1948, **24**:593-604.

The various theories concerning the etiology of acute pancreatitis are reviewed and discussed. From the literature, the authors conclude that the concept of etiology of acute pancreatitis (as enunciated by Wangensteen *et al*, and Rich and Duff) considers acute pancreatities, due to obstruction to the pancreatic ducts associated with an actively secreting gland, the most tenable one. The authors studied this problem experimentally by ligating the pancreatic ducts of cats and then stimulating the pancreas to secrete. The methods used to stimulate the pancreas to secrete were: feeding, stimulation of the vagus, injections of acetylcholine, pilocarpine and secretin. 64 cats were used in various experiments.

As a result of these experimental studies the authors stated that acute pancreatitis was the result of pancreatic ductal obstruction associated with an actively secreting gland. The degree of pancreatitis would depend then upon whether the obstruction to the pancreatic ducts was temporary or total, and whether or not the gland was actively secreting. The most extensive degree of acute pancreatitis was found with complete occlusion of the pancreatic ducts associated with an actively secreting gland.

M. O. CANTOR

The Treatment of Angina Pectoris by the Surgical Production of Adhesive Pericarditis, Thompson, Samuel Alcott, *Am. Practitioner*, 1948, **3**:81.

Relief of anginal pain following surgical production of adhesive pericarditis is due to two factors: (1) Establishment of an extracardiac collateral circulation from the adherent pericardium; (2) and production of myocardial hyperemia which leads to the development of a collateral circulation in the heart muscle.

Experimentally it has been shown that ligation of the left coronary artery in dogs produces an immediate mortality of 50 percent, but if the dogs are previously protected by instillation of talc powder in the pericardial sac, the mortality rate following ligation of the same artery is zero. It should be pointed out that the production of adhesive pericarditis is apparently not related to a constrictive pericarditis and is not reproduced by this experiment.

The treatment of angina pectoris depends on increasing the cardiac reserve. Any increase in the cardiac reserve beyond that which the patient has at rest, will diminish the severity of anginal attacks. The author describes an operation in which the left fifth costal cartilege is removed leaving the

perichrondrium behind. The internal mammary vessels are preserved. The pericardial sac is opened and 10 cc. of a two percent solution of novocaine is instilled into the sac. This is allowed to remain for five minutes and is then aspirated. Two drams by volume of sterile U.S.P. talc powder are now distributed widely over the visceral pericardial surface. Caking of powder is avoided. The wound edges are protected from the powder. Aside from a pneumonitis and clinical mediastinitis indicated by a temperature of 102 to 103 degrees, all symptoms subside and the patient is well in five to seven days.

Selection of the patient depends on a definite diagnosis of coronary disease with angina, lack of improvement after prolonged medical treatment, and an extreme degree of disability. Contraindications are congestive heart failure and an active myocardial infaret.

The mortality rate from the operation was 16 percent of 36 patients reported. Eighty-five percent of the patients were more than 50 percent improved and 70 percent of the patients showed marked improvement.

M. T. FRIEDELL

Isotopes in Neoplastic Disease. Lawrence, John H., *Rky. Mts. Med. Jr.*, 1948, **45**:980.

Isotopes have three applications in the problem of neoplastic disease: 1. the carcinogenic properties of irradiation apply to the irradiation emitted by isotopes as well as to that of x-rays or radium; 2. isotopes can be used as tracers in trying to learn more about the nature of the cancer cell, and 3. they can be used therapeutically as a source of destructive irradiation. In isotope therapy there is the problem of giving irradiation to the tumor cell without causing harmful irradiation to normal cells. The examples in which success has been achieved are enumerated.

The use of radioactive phosphate which localizes in bone marrow has been successful in the treatment of leukemia. The use of radioactive phosphate P32 has been noteworthy in management of polycythemia vera. The application of radioactive iodine has been helpful in management of hyperthyroidism. The use of filter paper saturated with sodium radiophosphate placed over warts, basal cell carcinoma and keratoses has given favorable results. The use of radioactive colloidal compounds which localize in the marrow, spleen, and liver have been useful as therapeutic agents in polycythemia vera and chronic myelogenous leukemia.

The author feels that the great contribution of radioactive isotopes is not so much as therapeutic agents as will be their use as tracers to study metabolic processes. GEORGE J. BAER

Surgery of Portal Hypertension. Learmonth, J. R., and MacPherson, A. I. S. *Lancet*, 1948, **2**:882.

This paper records the author's experience with surgical procedures to relieve 16 patients with symptoms of portal hypertension by means of venous shunts, or when portal obstruction was limited to the splenic vein, by splenectomy alone.

The patients were classified as follows:

	No. of cases
Group I: lienorenal venous anastomosis...	9
Group II: splenectomy (lienorenal venous anastomosis judged impossible).....	3
Group III: laparotomy only.....	1
Group IV: splenectomy for splenic thrombosis	3

In *group 1,* all had some degree of hepatic cirrhosis. Haematemesis was the only symptom in three of the cases; ascites was present at beginning of illness in three cases, but absent or minimal when haematemesis occurred; and in the remaining three both ascites and haematemesis were present. Two patients died after operation; one was a recent operation and not included in the series; and the remaining six were reviewed after postoperative periods ranging from four to twenty-three months. In none of the six had haematemesis recurred after operation. The authors were impressed by the improvement in the general condition of these patients—all had gained weight and returned to full employment.

In *group 2,* a lienorenal anastomosis had to be abandoned, usually because the renal vein was not suitable. There was no appreciable improvement in these cases. One died 26 days after operation. They do not recommend splenectomy in such cases, but consider it wiser to abandon the operation.

In *group 3,* laparotomy was only a palliative measure for ascites.

The anastomosis was performed by means of a 'Vitallium' tube. They have had no experience with end to side anastomosis. The chronic type of cirrhosis rather than the acute type offers the most promising results from this operation.

In *group 4,* the obstruction to the portal circulation was in the splenic vein and the presenting symptom was haematemesis, the haemorrhage being from dilated collaterals about the cardia which connect with the vasa brevia to the systemic circulation. The liver was normal in these cases, and splenectomy alone gave immediate uniformly good results.

D. J. LEITHAUSER

Cancer of the Rectum. Rankin, Fred W., *Rky. Mt. M. J.*, 1948, **45**:1023.

Cancer of the rectum is easily diagnosed by digital examination, proctoscopy and biopsy. Any case with blood in the stool warrants a proctoscopic examination.

The trend toward sphincter saving operations is unfortunate and there is now no proof of higher longevity and lower morbidity and mortality. The Miles operation is the greatest contribution to rectal surgery. A colostomy needs no defense.

Polyps of the colon and rectum are pre-cancerous lesions. Seventy percent of the cancers of the rectum and colon occur from the sigmoid to the anal canal; 71 percent of the polyps occur in the same area—a significant fact. In the case of a lone pedunculated polyp high in the rectum with a frozen section diagnosis of adenocarcinoma Grade 1 or Grade 2, one is justified in excising the polyp with a wide bit of mucous membrane around the base. When careful microscopic investigation shows no invasion of the base of the polyp, enough has been done.

Changes in bowel habit have been overstressed as presenting symptoms. Bleeding is a most frequent symptom which brings these patients to the doctor. Proctoscopic and digital examinations should be done before barium enema, and this should be done before barium is given by mouth.

It is suggested that the recto-sigmoid juncture be regarded as an area about two inches long, partially inside the peritoneum and partially below the peritoneum. For cancers which are not at least one to two inches above the peritoneum the Miles procedure is the most satisfactory, and all of those below this point should be operated upon by a radical procedure, preferably of the Miles type. When the lesion is more than one to two inches above the peritoneal fold, one is justified in doing a resection and restoration of continuity by suture.

The prognosis of cancer of the rectum is good. The average duration of symptoms is ten and one-half to eleven months. Of 167 cases, 62 percent were alive and well after three years and 57 percent after five years.

VICTOR T. HUDSON

The Nature of Lateral "Aberrant" Thyroid Tumors. Warren, Shields, and Feldman, J. D., *Surg. Gynec. & Obst.*, 1948, **88**:31-44.

The authors present 57 cases of lateral thyroid tumors of the neck. An analysis of their microscopic findings indicates that most of these lateral tumors are metastases from cancers of the thyroid gland. The primary cancer of the thyroid is not infrequently quite small and may be overlooked both clinically and at surgical exploration. The most usual cancer is that of the papillary type. Histologically, the lateral growths were identical with that of the primary. Surgical removal of the cervical lymph nodes and the thyroid gland must be complete to prevent local recurrence. This type of tumor has not been found to be associated with evidence of hyperthyroidism and generally they tend to occur in a younger age group.

W. R. LOVELACE

Indurated Leg and Leg Ulcers. Mahorner, Howard. *Surg. Gynec. and Obst.*, 1948, **88**:115.

Nine factors which influence the development of indurated leg and ultimately lead to leg ulcer are: 1. postthrombophlebitic edema; 2. varicose veins; 3. obesity; 4. trauma; 5. infection; 6. lymphedema; 7. immersion leg; 8. arteriovenous communications; 9. systemic causes. Usually two to four of the factors are responsible in any case of leg ulcer. Trauma is emphasized as is also the presence of trychophyton infection. Skin grafting is recommended for larger ulcers. Ligation of varicose veins is urged for therapeutic and not cosmetic reasons.

Conditions such as immersion foot and arteriovenous communications are discussed. Excision of subcutaneous tissue in lymphedema is advocated. Correction of various distant causes of poor circulation may help. The author favors dried blood cells as a dressing in conservative management of leg ulcers.

M. T. FRIEDELL

The Roentgenographic Appearance of Renal Cancer Metastasis In Bone. Sherman, Robert S., and Pearson, T. Arthur, *Cancer*, 1948, **1**:276.

Clinical and x-ray diagnosis of renal cancer metastases in bone is difficult. Some of the factors responsible for this difficulty is the tendency of some primary renal tumors to remain silent or grow rather slowly and the rather high percentage of solitary metastasis to bone (about 60 percent in this series). In an effort to improve the roentgenographic diagnosis of renal cancer metastases in bone, the authors reviewed 36 proved cases of such metastases from the files of the Memorial hospital for the Treatment of Cancer and Allied Diseases.

The metastases of renal cancer to the bone are characterized by the following feaures: the tumors are medullary in origin, oval in configuration, predominantly destructive to both medullary and cortical bone, and tend to form a periosseus mass. In tubular bones the position of the metastases was

always symmetrical, or nearly so. The boundary of the metastases is fairly apparent in many cases. Fifty percent of the cases are complicated by pathological fracture. The metastases have no significant predilection for any bone or any particular site in any bone. Periosteal reaction is rare.

There are three types of roentgenographic appearances: (1) lytic, (2) septate, (3) patchy, in order of frequency of occurrence. The lytic type is most predominant (75 percent in these series) and is characterized by predominant destruction of bone. The patchy type is characterized by fine patchy areas of medullary bone destruction. The lytic and patchy types are common appearances in a majority of cancer metastases to the bone of multiple primary origin. The septate form, which is characterized by an approximately equal degree of bone production and bone destruction, with an internal pattern made up of dense septa forming loculations, is sufficiently distinctive to warrant suspicion of a renal origin for the primary tumor. In some of the primary lytic types of bone metastases delicate, indistinct and incomplete septa can be seen, which may be helpful in arriving at a correct diagnosis.

Mention is made of the occasional pulsating bone metastases of renal cancer.

W. R. LOVELACE

The Treatment of Ruptured Liver with Absorbable Hemostatics. George W. Papen, and Stanley Mikal, *New England J. Med.,* 1948, 239-920.

Three cases of liver rupture by non-penetrating violence are described in detail. In each case the diagnosis was made preoperatively, and the continuing hemorrhage was successfully arrested by the use of packs of oxidized cellulose, alone or in combination with strips of gelatin sponge. "In all cases relatively complete hemostasis was obtained three to five minutes after the laceration had been packed with oxycel and gelfoam and gentle pressure applied. No secondary liver hemorrhage ensued postoperatively. . . . Postoperative biliary peritonitis or fistula never developed when the abdomen was closed without drainage."

The management of these cases is reported in detail because previous reports of the use of absorable hemostatics for liver hemostasis were mainly concerned with animal experimentation. Other methods of control of liver bleeding involve attempted suture of liver parenchyma or the packing of the defect with muscle, omentum or gauze. The history of surgical hemostasis is outlined. Animal fibrin was used as early as 1915; the present absorbable hemostatics were only lately developed.

The incidence, mortality, coincident depression of function and classification of liver trauma are discussed. It is obvious that the high mortality which has been attached in the past to non-pentrating injuries of the liver has been due to delay in exploration and to postoperative infection. Ample supplies of blood, avoidance of drains, and adequate use of penicillin, combined with hemostatic methods not involving further damage to liver tissue should reduce mortality. It is interesting to note that each of these three patients had preoperative scout films, both chest and abdomen, preoperative blood and fluids, gas-gangrene and tetanus antitoxin. It is not stated that penicillin was given preoperatively. The postoperative course of the patient who had drainage of the peri-hepatic region was startlingly different from that of the other two. The conclusion states that closure without drainage is better. LOUIS RIVERS

Treatment of Pruritus Vulvae by Local Inunctions with Pyribenzamine. B. Zondek, and Y. M. Bromberg, *Acta Med. Orientalia,* July-Aug. 1948, 7:123.

This work was conducted in Rothschild Hadassah University Hospital, Jerusalem. It is brought out that the etiology of pruritus vulvae presents a definite problem and all factors local and general must be studied.

Two patients suffering from pruritus vulvae due to allergy to endogenous hormones were treated by oral administration of anti-histamine substances. No effect on itching was noted. Then pyribenzamine was applied locally on the vulvar region, glycerine was chosen as the most suitable vehicle and pyribenzamine being soluble of anti-histamine drugs.

Fourteen patients from various etiologic factors were treated by local applications of three percent pyribenzamine in glycerine in various forms, every eight hours. Six cases of itching receded completely; seven cases improved; one unimproved.

The mechanism of action of local application is discussed. It is emphasized that the effect is symptomatic only and last only as long as inunctions are continued. EDWIN L. ZANDER

In Memoriam

ANGELO ADAM GALLO

M.D., A.I.C.S.

Dr. Angelo A. Gallo, 48, died recently at Pottstown, Pa., and was the first local surgeon to be elected to the International College of Surgeons. He graduated from the Hahnemann Medical college, Philadelphia, in 1926. Following his internship at the Hahnemann hospital, he went to the University of Vienna for a year of postgraduate study of surgery. Dr. Gallo began his medical career at Pottstown in 1934 as chief surgeon at the Memorial hospital, and after four years was transferred to the Pottstown hospital. One of the surgeon's proudest accomplishments was the development of the Women's Cancer Detection clinic at the Pottstown hospital, which he headed until his death.

MATTHEW JOHN HOENIG

M.D., F.I.C.S.

The field of coloproctology lost one of its valued contributors in the death of Dr. Matthew J. Hoenig, of Rochester, N. Y. Dr. Hoenig graduated from the University of Buffalo Medical School in 1919 and took his postgraduate work at the New York Polyclinic from 1928 to 1929. His hospital positions consisted of being attending senior coloproctologist at St. Mary's hospital, Rochester, 15 years; attending senior coloproctologist, Highland hospital, Rochester 15 years; and consulting proctologist, Monroe County hospital, 13 years. Dr. Hoenig was also a member of the American Medical Association, New York State and County Medical Societies, Rochester Academy of Medicine and the Rochester Pathological Society.

MIKLOS TEMESVARY

M.D., F.I.C.S.

It is with deep regret that we record the death of Miklós Temesváry, of Budapest, Hungary. A great force in establishing relations between the International College of Surgeons and the Hungarian surgeons and gynecologists, Dr. Temesváry received his education at Budapest, Breslau, Hamburg, and Pées and graduated in 1922. He acquired his obstretrical and gynecological operative practice while training at Dresden, Direnze, and Breslau. Since 1927 he developed his activity at Budapest, at the Weiss Alice hospital and was appointed its director in 1947. The surgeons and gynecologists of the world have lost one of its most devoted and esteemed contributors.

WILLIAM J. CARSON

M.D., F.A.C.S., F.I.C.S.

Dr. William J. Carson of Milwaukee, Wis., died Feb. 14, 1949 at the age of 56. Dr. Carson was born in Pittsburgh and attended the Pittsburgh academy, the University of Pittsburgh and the University School of Medicine. In World War I, he served with the medical corps as a lieutenant at Fort Snelling, Minn., at the Rockefeller Institute and for several months overseas. After the war he became associate professor of pathology at the University of Maryland. Dr. Carson, Fellow of the International College of Surgeons, was also a member of the American Medical Association, the Wisconsin State Medical Association, and the Milwaukee County Medical Association.